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Symposium: The Rôle of Wild Life in the Dissemination of Disease

1.—General Introduction and Some Veterinary Problems

BY

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Compton, Berks.**

SUMMARY.—An account is given of some of the causes of morbidity and mortality in free-living wild life, and the possibility is discussed of wild mammals and birds acting as reservoir hosts for a variety of infections communicable directly or indirectly to domestic stock in this country and abroad. The need for further research is stressed since it is believed that additional information might be of considerable value to those interested in agriculture, nature conservation, veterinary preventive medicine and public health.

UNTIL about 30 years ago, the study of disease in free-living wild life was confined to a few conditions of very obvious importance to domestic animals and man. At that time scant attention was paid to the possibility that certain species of wild animals might be affected, quite independently, with their own specific diseases and might also act as reservoir hosts for a variety of pathogens without showing any symptoms of disease themselves. Mainly as a result of certain species of small wild mammals being adopted for use as experimental animals in research laboratories, information began to accumulate concerning mortality in these populations; but the main impetus to research came from Elton's classic paper in 1931 in which he described the existence of a large unexplored field in "diseases of wild life" and urged that further investigations be made. The link between the occurrence of disease under natural conditions and the marked periodic fluctuations in some wild animal populations is now established, although due allowance must, of course, be made for other factors associated with mortality, such as climatic conditions, availability of food, predation, and even stress. Fortunately, increased attention is being paid to this subject in many countries and the whole question of disease in wild life is now falling into line with similar investigations of the disease problems of man and the domestic animals.

Nowadays, in a small island such as Britain, nearly all our wild species are influenced to a greater or less extent by some form of human activity. This is not always so in other countries, but even in North America with its vast spaces and abundance of natural habitats, the impact of modern farming techniques is making itself felt on the well-being of the natural fauna. There is a growing tendency when such a situation arises, to establish national parks or refuges to guard, against extinction, certain inherently interesting species of wild life adversely affected by man. When this is done, new problems immediately arise and it has been clearly demonstrated, on more than one occasion, that breakdowns in disease control amongst cattle and sheep grazing in such designated areas could be attributed to the presence of infected wild life hitherto presumed to be healthy (Katz, 1941).

Economic Aspects

Various groups of individuals and organisations are affected directly or indirectly by this problem of disease in wild animals; game preservation is a good example. Game, as everyone knows, or should know nowadays, can be of considerable value on a farm or estate. The farmer may harvest this crop himself, at the same time enjoying the sporting facilities, or he can let the shooting rights on his land. As the value of such shooting may reach the figure of 10s. per acre in many areas, it provides a useful additional income without much outlay. It is worth recalling that many years ago "grouse disease" in Scotland was considered worthy of special investigation by a Royal Commission (1911) because of the economic value of the grouse. Another commercial enterprise, namely, fur trading, has always been much concerned with fluctuations in animal populations. The snowshoe rabbit enquiry, conducted over many years from Oxford, showed quite clearly the importance of enzootic disease as a limiting factor in the numbers of

* Papers presented to the Annual Congress of the British Veterinary Association in Oxford on Friday, September 8th, 1961.

this particular species, this in turn influencing the number of fur-bearing predators from season to season. The returns of the Hudson's Bay Company over a prolonged period do, in fact, show interesting trends in those populations and it is now possible to predict good and bad trapping years by a study of the relevant statistics.

The Link with Ecology and Preventive Medicine

The student of pure or of applied animal ecology is naturally interested in these phenomena, but many of the fluctuations in numbers of some species, particularly the smaller mammals, are still not adequately explained. In this country much of the mortality in the vole population which has a cycle of about 4 years, could well be associated with disease: toxoplasmosis is common in voles (Findlay & Middleton, 1934) and also pseudotuberculosis caused by a Pasteurella. In addition, they have their own specific infection with an acid-fast organism long associated with the name of the late Dr. Wells, of Oxford (Wells, 1937). This is indeed a most interesting organism in that not only does it cause epidemic disease in voles but it has also provided a useful antigen for man and animals against tuberculosis, similar in many ways to B.C.G. vaccine but with perhaps more "fixed" characteristics. This strain has been employed both in this country and abroad in the prevention of tuberculosis and its use for this purpose constitutes an indirect benefit arising from the investigation of disease problems in wild life. Similarly, in moles there is a pronounced mortality about every 6 years and a specific mycotic disease, hitherto never observed in any of the domestic animals or man, has been shown to be associated with this mortality (McDiarmid & Austwick, 1954). This disease, known as haplosporangiosis, produces a granulomatous type of lesion in the lungs. In addition, from such granulomata, we have isolated an aerobic actinomycete which is pathogenic for mice. Again, this phenomenon is associated with further interesting possibilities. Dr. Jellison in the U.S.A. has devoted much time and effort to the investigation of haplospor-angiosis in wild mammals; he has found it in a variety of species in different countries and has postulated the theory that haemorrhagic fever, an important disease of unknown aetiology in man in some areas, particularly Korea, might well be associated with this type of mycosis (Jellison, 1954).

Puffinosis

In wild birds much interesting information has come to light during recent years, in that specific infections have been discovered quite distinct from those associated with poultry. For example, a virus infection, known as puffinosis, which has not been described in domestic stock, has been found to be associated with mortality in manx shearwaters on the islands of Skomer and Skokholm off the Welsh coast (Surrey Dane, 1948) and, to a lesser extent, in herring gulls and blackheaded gulls elsewhere. It was found that the infecting agent of this disease, which is characterised by vesicles on the webs of the feet, conjunctivitis and sometimes lung lesions, was transmitted from bird to bird by the characteristic habit of young shearwaters of using the same stones for perching on during their early attempts at flight; this is a good example of the solving of a problem by the combined efforts of ecologists and virologists. It has now been shown that the disease can be established experimentally in young domestic ducklings.

Other Epidemiological Factors to Consider

When considering the risks to human health and to farm stock from foci of infection in wild life we must pay considerable attention to the ever-increasing freedom of transport between the nations; the constant development and reclaiming of vast tracts of virtually uninhabited land in different parts of the world where wild fauna may harbour infections such as leishmaniasis or plague has already brought its own problems. Perhaps one of the best examples of the value of epidemiological studies in the wild life-to-man relationship came to light some years ago with the occurrence of ornithosis in the fulmar petrels in the Faroe islands. Man became infected and thus here was a clear-cut instance of the danger of direct contact with an infected free-living host; since then, ornithosis has been confirmed in a variey of species of wild birds quite apart from the psittacines. The feral pigeons in London and other large cities are also commonly infected and must act as a constant reservoir of virus.

The Contamination of Water Supplies

Water supplies are frequently contaminated by wild species. For example, outbreaks of *Salmonella typhimurium* infection in sheep in Australia have been traced to infected magpies and foxes frequenting the water holes (Watts, 1951). In addition, tularaemia is recognised as a grave health hazard in certain countries, particularly North America where the disease is rife in the local beaver and muskrat populations (Jellison, Epler, Kuhns & Kohls, 1950). Often mountain streams, thought to be of impeccable quality, are contaminated with the carcases of such animals.

Meat Inspection of Game

So far as meat inspection is concerned, it is common knowledge that putrefaction is the main reason for the condemnation of game and wild birds. Little attention is paid to other conditions, although in the London markets, wood-pigeons are checked by an incision over the liver; if there is evidence of disease in the form of "spots" in this tissue, the bird is discarded. Infection with the paracolon group of organisms has been cited in the medical literature as a well-established cause of human illness and a disease of this type has been confirmed in partridges and wood pigeons (McDiarmid, 1953)—birds often used for human food. It is of interest here to point out that paracolon bacilli were isolated from wild birds on a farm in Berkshire where some trouble had been experienced with the B.W.D. testing programme in poultry and doubtful reactors had occurred to the agglutination plate test; when the paracolon strains were inoculated into experimental fowls, these re-

acted, in a doubtful manner and only for a short period, to the B.W.D. test. Again, this example serves as an illustration of the possible links, sometimes quite unsuspected, between wild life disease and veterinary investigations.

The Arbor Viruses

Perhaps the most important group of virus diseases in free-living animals are those transmitted to man and the domestic animals by arthropods. There can be no doubt that the real reservoirs of the causal agents of equine encephalitis, Russian spring-summer encephalitis, Murray Valley encephalitis and West Nile encephalitis, to mention only a few, are free-living wild hosts and that the infections they produce in man and farm livestock are purely biological accidents.

Fortunately in this country we are not called upon to cope with any of those infections but we do have louping-ill, and one cannot help wondering if perhaps wild hosts exist for this virus. Again it may be that the sheep are infected by accident and that the real host or hosts for the virus exist elsewhere. The field vole is susceptible to experimental infection but there is no record of free-living voles in the "louping-ill" areas being tested for antibody or for the presence of virus. The red deer seems another possible host and although a limited search for antibody in stags shot during the stalking season proved fruitless (Wilson, 1952), Dunn (1960) subsequently demonstrated the presence of antibody in deer blood collected from various areas in Scotland.

Protozoal Problems in Britain

One sometimes wonders if the occurrence of redwater in cattle might be linked to the presence of deer in the vicinity. Anaplasmosis has been demonstrated in deer in other countries (Boynton & Woods, 1940) often associated with the presence of the disease in neighbouring cattle, and again I know of no investigation along these lines in Britain despite the fact that the highest incidence of redwater in cattle coincides with a high deer population and the presence of ticks. In addition the rôle of deer in the epidemiology of tick-borne fever, a rickettsial disease of sheep, might also be well worth investigating on the hill farms in Scotland.

Diseases of Major Importance

Some diseases of major importance including those notifiable in Britain, are common in wild species. Rabies, rinderpest, blue tongue and many of the infections associated with trypanosomes all occur in various species of wild mammals abroad, and malarial parasites are common in a variety of wild birds. Foot-and-mouth disease is present in the deer population in several European countries and we were extremely fortunate in that it did not gain access to the Scottish red deer population during the past winter. It did, of course, occur in fallow deer many years ago at Woburn Park, and hedgehogs and rats have also been found naturally infected. Although such natural infections are apparently rare in our native mammals, birds, especially starlings, have been incriminated on very strong circumstantial evidence, of the passive transfer of virus from the continent during migration (Wilson & Matheson, 1952).

Wood-pigeons as a Source of Mycobacterial Infection

Bovine tuberculosis has now been eradicated from our herds but the problem of avian infection is still with us and from time to time can cause considerable trouble in the pig industry. Undoubtedly, nowadays, the majority of our avian infections in pigs and cattle arise from direct or indirect contact with wild hosts, the wood-pigeon probably being the culprit in most instances (McDiarmid, 1948). A few years ago we had a severe outbreak in our pigs at Compton clearly associated with the contamination of new leys by large numbers of wood-pigeons, 4 per cent. of which had macroscopic evidence of the disease. In addition, there is always the effect of the presence of this infection on the tuberculin testing programme in pigs and cattle, and, of course, the ever present risk of domestic poultry acquiring infection. One of the interesting features of avian tuberculosis in wood-pigeons is the character of the strains of causal organism. In addition to the ordinary smooth type, we also encounter a rough variety which has many of the characteristics of *Mycobacterium johnei*; it is extremely difficult to cultivate, several months elapsing before growth can be seen, and it will only grow initially on a Johne medium such as Finlayson's. On primary isolation it will not kill young cockerels by the intravenous route. However, this species, if passaged in domestic fowls, reverts to the smooth type, grows readily on ordinary avian medium and regains its pathogenicity for this species. This is indeed an interesting situation and one cannot help wondering what would occur if we inoculated this rough strain into young susceptible calves, or for that matter what would happen to *Myco. johnei* if passaged rapidly through fowls.

Brucellosis

Brucellosis in this country has so far been mainly a problem of cattle and man, although some evidence of its occurrence in wild deer (McDiarmid, 1951) and in rats (Bosworth, 1937) is available. However, in Denmark the true host for *Br. suis* is the brown hare and "pockets" of infection exist. The pigs derive infection from the hares either by grazing contaminated paddocks or by direct ingestion of an infected carcase (Bendtsen, Christiansen & Thomsen, 1954). In Switzerland and France brucellosis is common in hares (Jacotot & Vallee, 1951), usually the *melitensis* type or even *abortus* and there seems to be no reason why our hares should not acquire this infection, given the opportunity. We have examined several hundred sera from hares in Berkshire for Brucella agglutinins with negative results, but bearing in mind the Danish findings, sampling might have to be done over a very wide area before a "pocket" of infection was located. Some of the unusual outbreaks of so-called *Br. melitensis* infection might even be traced to hares. So far no one has investigated this possibility although in some outbreaks a feral source of infection has been suspected.

Some Other Diseases of Hares

The hare is, in fact, a biological museum so far as diseases are concerned. Already coccidiosis, pseudotuberculosis (pasteurella), aspergillosis, staphylococcal pyaemia and streptococcal endocarditis have been confirmed in British hares. Moreover, this species appears to be particularly susceptible to helminth infestations, and other conditions encountered have included "orf"-like lesions which have often been confused with myxomatosis and a "braxy"-like disease causing sudden death, especially on lucerne lays. This latter condition even produces the characteristic inflammatory zone in the stomach as seen in sheep, but so far no bacteriological examinations have been made. Toxoplasmosis is common in hares in Sweden (Borg, 1953) and other Scandinavian countries and with further search, might yet be discovered in British hares; if so, this would provide an interesting link with the infection in sheep and also in man. It appears as if sheep and hares have many diseases in common and perhaps it would be well worth while, from the comparative epidemiological point of view, to investigate mortality in hares on a larger scale than has hitherto been done.

Leptospirosis

Leptospirosis in dogs, and for that matter in man, is often associated directly or indirectly with the rat population—at least 50 per cent. of rats are carriers of *Leptospira icterohaemorrhagiae* and thus an opportunity does exist for dogs, especially in country districts, to acquire infection. So far no natural reservoir host has been described for *Lepto. canicola* in Britain and the dog is still presumed to be the principal source of infection. However, little has been done in this field and it is worth remembering that jackals in the Middle East have been found naturally infected (Van der Hoeden, 1955); we know that our native red fox is frequently infected with *Lepto. icterohaemorrhagiae*, presumably from the rats which form a major part of its diet, and further investigation might even reveal the presence of *Lepto. canicola* as well. The possibility of the existence of feral hosts for other leptospiral infections in Britain has not been investigated although many infections with various strains have been recorded in a great variety of small rodents in other countries, particularly in Italy (Babudieri, 1953).

Listerellosis

Listerellosis has come to the fore as an important sheep disease in Britain and recently we found this infection in partridges in the vicinity of an infected flock of sheep. Listerellosis has been found in capercaillie and blackgame in Sweden (Lilleengen, 1942) but apart from the partridges I am not aware of any record of its occurrence in game in this country. The capercaillie in West Perthshire might, however, be worth investigating. They were reintroduced to this area from Sweden many years ago and might, conceivably, have brought this infection with them. Erysipelothrix infection sometimes occurs in hill sheep without any evidence of association with pigs. It is, perhaps, significant that this organism has now been isolated from the Scottish red grouse and thus this species might play an important rôle in the epidemiology of the condition in those remote areas.

Salmonellosis

Salmonellosis is widespread in wild rodents; and contamination of feeding-stuffs frequently results from such infections. Several types have been identified and the commonest are probably *S. typhimurium* and *S. enteriditis*. The latter species has also been isolated from hedgehogs. In addition, *S. gallinarum* has been recovered from rooks in Yorkshire and evidence was presented to show the probable association of these cases with local outbreaks of fowl typhoid on neighbouring poultry farms (Harbourne, 1955).

Infectious Sinusitis

Last year considerable concern was expressed in sporting circles at the occurrence of infectious sinusitis in pheasants and to a lesser extent in partridges. The mortality rate on some estates was high and certainly such mortality had not been encountered in previous years although isolated cases of this disease had been described. There is now ample evidence to show that this disease is caused by a pleuropneumonia-like organism and that it is similar, if not identical, to infectious sinusitis of turkeys. During these investigations fowl pest antibody was also detected in pheasants and, as the actual virus was isolated from wild birds in Britain some time ago (Wilson, 1950; Blaxland, 1951), these findings must be considered when formulating any future control policy for this particular disease.

Histomoniasis

Blackhead due to *Histomonas meleagridis* still remains a problem so far as partridges are concerned. Frequently we encounter cases in downland areas far removed from any possible contamination from domestic fowl. In some seasons the mortality may be quite high and numerous dead or dying birds are found. With natural infection present in the partridge stock the risk of introducing susceptible birds such as turkeys into these apparently ideal surroundings would be considerable.

Endoparasitis

So far no mention has been made of diseases due to endoparasites. These are numerous in many different species of wild birds and mammals. It is, however, not always easy in wild species to know where normality ends and disease begins. For example a heavy *Raillietina* infestation in an emaciated wood-pigeon leaves one in no doubt, but the presence of *Syngamus trachealis* in a plump young rook still in the nest, is not so easy to evaluate. It seems to me to be of considerable interest that susceptibility varies so markedly from species to species and probably a number of factors are involved. The young rooks are apparently almost unaffected by a *Syngamus* infestation which would, for example, have a disastrous effect on young pheasant poults. The caecal worms of the partridge and the grouse still present a prob-

lem but perhaps not to such an extent nowadays, with the stocks of these birds not so heavy as they used to be.

In wild mammals a great variety of helminth infections exist; perhaps among the most interesting is the liver fluke in the rabbit. In this instance it is perhaps worth noting that the contamination of watercress crops and the consequent accidental infection of man need not necessarily always be attributed to infected domestic stock. Many types of lungworm occur in a variety of species; among the most interesting are the *Crenosoma* species in the hedgehog and shrew and the so far unidentified species in the mole. Such natural infections in small animals, suitable for use in the laboratory, might even be of some value in assessing methods of immunisation and/or therapy.

Dr. Dunn of Glasgow is at present engaged in some very interesting work on the classification of the endoparasites of deer and the study of possible interrelationships between these parasites, their natural hosts, and the sheep and cattle grazing in the same area. In addition the effect of the social behaviour of the various types of deer on the parasite burden is being examined.

Ectoparasites

Ectoparasites seldom cause obvious disease in wild life apart of course from those diseases they transmit. I have, however, seen mortality in young grouse due to ticks and in young partridges due to heavy louse infestation. Large numbers of mites aggregating in the respiratory system can also sometimes cause the death of young birds; I have seen partridge chicks killed in this way.

Neoplasms

Neoplasms are extremely rare in wild life. This is probably due to few wild species living long enough for such conditions to develop. Those recorded have occurred mainly in rabbits, deer and whales. The first 2 species are affected principally with the transmissible types such as myxomatosis and papillomatosis respectively and there appears to be a close relationship between the wart-like lesions found in deer and the similar condition encountered in cattle. However, no cross-transmission experiments have so far been attempted although the condition in deer can readily be transmitted to other animals of the same species (Shope, 1955). The whales exhibit the more classical types of tumours such as fibroma, adenoma, and ganglioneuroma (Rewell & Willis, 1949). Tumours in birds are extremely rare apart from leukaemic conditions similar to those encountered in domestic poultry. With the increased availability of radioactive substances, we may yet encounter further evidence of this type of disease in wild animals. In fact evidence of radioactivity above the normal level has already been detected in redshanks shot in the South of England and this preliminary finding has triggered off a series of investigations into the possibility of migrating birds, acting as detectors of radioactive substance.

Toxic Chemicals

Again, although perhaps not strictly in accord with the purpose of this paper, the numerous deaths attributed to the use of seed dressing and sprays which have occurred in recent years, in wild birds and in predators such as foxes should be mentioned. Opinion is at present sharply divided. On the one hand we have an eminent scientist (Slater, 1961) stating that "we cannot sacrifice the efficiency of our food production in order to avoid the loss of a few birds and mammals killed by chemicals, a loss which is only a minute fraction of those due to natural causes or the guns of sportsmen." On the other hand the British Trust for Ornithology, the Royal Society for Protection of Birds, the Nature Conservancy and the Game Research Association, quite apart from innumerable private individuals, are all very perturbed about the matter. It is perhaps a relief to know that the deaths of foxes which have followed much the same pattern as the deaths of birds have now been attributed to a "carry over" of the same type of poison from the affected carcases, and not to an infectious agent as was previously suspected (Taylor & Blackmore, 1961). At least the opportunity to put matters right without much difficulty is still in our hands, whereas if an infectious agent had been responsible it would have been a much more difficult problem to cope with.

The Need for Further Investigation

Undoubtedly, far more attention should be paid to the position of wild life in epidemiology. The only available information accumulated in this country in recent years, has resulted from the efforts of a mere handful of individuals engaged on other duties and investigating the problem in a part-time capacity. The U.S.A. and the Scandinavian countries have already recognised the importance of such work and now possess well organised research services for this purpose. Switzerland has even its own Institute for the study of disease in game, and France and Germany are also well ahead of us in this matter.

So far, in this country, little interest has been shown in this problem by official bodies, and yet one disease, namely myxomatosis in rabbits, caused far-reaching repercussions in the whole economic pattern of farming in Britain in the space of 2 or 3 years. Prior to 1953 I am sure no one would have considered that such a thing could happen.

There can be no doubt, from the evidence available, that, in the interests of farming, nature conservation, veterinary preventive medicine and public health, this subject is worthy of greater interest than it has hitherto received.

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2.—Ecology of Diseases in Wild Mammals and Birds

BY

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SUMMARY.—Wild mammals and birds have many diseases and provide reservoirs of infection which may pass to domestic animals and man during epizootics. Fluctuations in the abundance of species are considerable and disease is only one among many causes of mortality. With reference to the principal zoonoses, plague, rabies and tularemia in the U.S.A. are considered, especially in their sylvatic aspects, and in each case the need for joint investigations of the diseases by ecologists and pathologists is evident. Individual studies of diseases of wild-life have been carried out in Britain; there is need for more work and some centralisation.

THERE are still many who think of primitive peoples and wild animals as sharing a ruder, more vigorous, life than ours, less prone to either physical or mental ailments. Ecological research, particularly during the last 30 years, has steadily disabused us of such naïve thinking. Readers of Charles Elton's *The Ecology of Invasions* (1958) are reminded that bubonic plague is enzootic among the gerbilles living on the South African veldt and that, during an epizootic, the bacteria can pass *via* a flea to the multimammate mouse and so to domestic rat and man (Davis, 1953). Similarly, in western U.S.A. and Canada sylvatic plague is widespread among ground squirrels and other rodents, although human outbreaks are rare (Link, 1955).

References to diseases in wild mammals and birds, in the free state and in captivity, are legion and a bibliography compiled by Halloran (1955) lists some 18,000, culled from 900 different publications covering the period 1830-1950 : and this is after the intentional omission of all references to rabbits, rats and hamsters. Many papers on diseases of free-living wild animals are critically reviewed by McDiarmid (1960).

A wild animal population does not increase indefinitely, although it can expand explosively if introduced to a new and favourable environment, and it is evident that the abundance of a species is checked by a mortality related to its density in a particular habitat. But the causes of this mortality and the nature of population dynamics have been much in dispute and some of the arguments have not been without their philosophical content (Solomon, 1949 ; Nicholson, 1954 ; Thompson, 1956). Much population research has been on insects, but Lack (1954) studying birds, believes that populations are limited by food shortage, predation or disease, separately or in combination. His emphasis is on food shortage but, in the case of mammals, unfavourable weather and adreno-pituitary exhaustion are equally likely to be of importance (Chitty, 1955 ; Christian, 1957). In a later paper, Chitty (1960) has pointed out that the offspring of animals adversely affected by their environment may themselves be more susceptible to natural hazards. Since an animal's environment includes other individuals of its own species, besides food, cover, predators and weather, the effects of intra-specific strife may exercise considerable influence.

Much of Chitty's work has been on the field vole (*Microtus agrestis*), populations of which often show a recurrent high mortality at about 4-year intervals.

Infectious disease was at one time thought to be responsible, particularly after the discovery by Wells (1937, 1946) of vole tuberculosis (*Mycobacterium tuberculosis*). Some mortality from tuberculosis was postulated, but the disease was not found to have any marked effect on the survival of voles in the laboratory, nor was there any clear correlation between the incidence of tuberculosis in the field and fluctuations of vole numbers (Chitty, 1954).

While disease may clearly affect the numbers of an animal population most strikingly, well-adapted parasites do not usually produce disease and death in reservoir hosts. It is when a parasite enters aberrant hosts that epizootics and epidemics occur; as when plague bacteria are introduced into black rats, brown rats or ground squirrels, tularemia into wild rabbits, or rabies virus into foxes, coyotes or skunks. Even so, the aberrant host—if it is a biologically successful species—is not completely exterminated. Perhaps the best example is that of the myxoma virus, benign in cottontail rabbits but causing a 99.8 per cent. case-mortality in fully susceptible wild European rabbits, which has nevertheless not eliminated rabbits either in Australia or Europe.

There is a convenient listing of the principal zoonoses in the WHO/FAO Reports (1951; 1959), under viruses, rickettsia, bacteria, fungi, protozoa, helminths or ectoparasites, and a proper appreciation of the numerous wildlife reservoirs of disease. Only a few of these can be referred to here.

The occurrence of plague in the United States is particularly interesting. The bacillus probably arrived in the U.S. in the last years of the nineteenth century (Link, 1955) in infected rats leaving ships on which cases of human plague had been notified, and there were epidemics in San Francisco in 1900 and 1907 and subsequently in other cities. Epizootic plague in rural areas of California was suspected in 1903, when there were occasional cases of plague in man, associated with the killing and eating of ground squirrels (*Citellus beecheyi*), which are widely distributed throughout the state. There were further deaths in 1908, including a case in Los Angeles when a boy was bitten by a ground squirrel and plague-infected squirrels were found. This was the first evidence of plague infection in wild rodents in the U.S.A. and resulted in a campaign aimed at eradication of this focus. Plague prevention measures had previously been confined to the destruction and examination of rats and general sanitation measures, but from 1909 onwards hundreds of thousands of ground squirrels, and much smaller numbers of other wild mammals, were examined at the federal plague laboratory. In an effort to maintain squirrel-free zones around cities, millions of the rodents were poisoned, gassed and shot by land holders and by state-employed mobile crews. The magnitude of the task of squirrel eradication was gradually realised and, about 1921, budgetary restrictions limited the hunting operations to locate plague foci, and the squirrel control work.

The first case of human plague of sylvatic origin outside California occurred in Oregon, in 1934, and stimulated the search for new plague foci, which have been found in wild rodents in 15 western states and as far east as Kansas. In spite of the development of more deadly poisons and more effective methods of rodent control, it is not economically possible to eradicate the disease in any of the known infected species over an area of millions of acres, even if the risk of complete destruction of wildlife were acceptable. As in South Africa, the best method of plague control remains the adequate control of domestic rodent populations and the prevention of epizootics among them. Many aspects of the ecology of wild-rodent plague remain obscure and will repay investigation.

Rabies is well known to be primarily a disease of wild carnivores of the families *Mustelidae* and *Viverridae* (Johnson, 1959) and the social importance of human rabies draws attention to what is a side issue of the normal cycle. The numbers of rabid wild animals attacking man are not a true index of the relative extent to which the wild species are affected, and in south-eastern U.S.A. where the grey fox (*Urocyon cinereoargenteus*) is an important rabies virus reservoir, epizootics can occur among foxes without a single human or domestic animal being affected in adjacent farming areas. (Jennings *et al.*, 1960; Scatterday *et al.*, 1960). The position was stated by the WHO Report of 1950 which recognised that rabies exists in 2 epidemiological forms; the first a widely disseminated disease propagated mainly by dogs and predominantly in urban regions, and secondly a more localised disease of wild animals, particularly wolves, foxes, jackals, vampire bats and mongoose. In 1953 rabies was first identified in insectivorous bats in the United States and has since been reported in 8 states, more recently in the freetail bat *Tadarida mexicana*, which migrates to Mexico in the autumn. To understand the ecology of rabies, further knowledge of the relationships between normal foxes, skunks and house cats is needed and the behaviour of these species towards rabid raccoons and bats. Regarding the wild fauna, there are 2 theories of rabies control, one being to eradicate the wild host, the other to contain the epizootic and allow the disease to kill itself out. Since it is seldom possible to eradicate wild populations completely, and the effort to do so may disperse rabid animals over a wider area and increase human contacts, the policy of containment is to be preferred.

A final example from North America concerns outbreaks of tularemia. Parker *et al.* (1951), reporting studies in the north-western U.S., refer to the beaver (*Castor canadensis*) and musk rat (*Ondatra zibethica*) populations in Bitter Root Valley, Montana, affected by epizootic tularemia; many hundreds of deaths being due at least in part to the disease. Many marshes and ponds were depopulated by March, 1943, and there were 8 cases of infection among local trappers who had skinned dead musk rats. Human infection with tularemia associated with deaths of musk rats are reported from Idaho, Wyoming, Oregon and many eastern States, and it is thought that the infection of beavers and musk rats is a reflection of concurrent epizootics among land mammals such as mice or voles and that water, or

mud, is the medium through which the infection is conveyed. The authors stress the need for careful joint investigations of the disease by ecologists and pathologists.

The significance of wild mammals and birds in spreading diseases has been appreciated in Britain for many years, but studies of diseases in wildlife have not been accorded any high priority by official bodies and have been carried out as incidental research by a number of individuals. The following may be noted: a study of helminth parasites in some wild birds, over 10 years (Clapham, 1957); the arrangements made by the British Trust for Ornithology to gather information about disease in wild birds and reported by Jennings and Soulsby (1954-61); studies by Wilson (1960) particularly on avian tuberculosis; by Ash (1957); the well-documented survey by Keymer (1958) and the continued interest of McDiarmid (1960). McDiarmid pointed out that bovine tuberculosis may be carried by wild pigs, deer or rats and that avian tuberculosis occurs in many species of birds, particularly in the wood-pigeon in Britain (incidence of 2 to 4 per cent. annually). Where pigeons feed or drink with domestic poultry there is thus some risk of infection.

There seems little doubt that deer may be a natural reservoir of the virus of foot-and-mouth disease in continental Europe, and it has frequently been suggested that migratory birds might carry the disease to Britain (Wilson & Matheson, 1952). Since initial cases of foot-and-mouth disease on the south-eastern coast of England occur at the places where migrant starlings make their landfall, there is circumstantial evidence against these birds, and some gulls, which also associate with grazing cattle and sheep. On the other hand, since birds are resistant to the virus, they could only carry it mechanically and this has not so far been demonstrated, although several hundred starlings from infected farms have been examined.

McDiarmid (1955) recorded *Staphylococcus aureus* in a wild brown hare and thought the strain to be one commonly associated with mastitis in the dairy cow. Also Jennings (1954) described similar strains of staphylococci from the hawfinch and the green woodpecker.

Species of Salmonella are carried by rats, mice and voles and have been isolated from the magpie and curlew (Jennings, 1954) and rook (Harbourne, 1955). The rooks in the last case are thought to have been associated with the widespread outbreak of disease among domestic poultry.

Brucellosis is now known to occur in several species of wild mammals, for example, hares in Denmark (Thomsen, 1959), and an investigation by McDiarmid (1951) showed that fallow and Japanese deer reacted to a blood agglutination test, indicating that they could be a reservoir of this disease.

Keymer (1958) surveyed the mortality of 513 British birds examined between March 1st, 1954, and October 31st, 1957. Natural hazards, violence, poisoning and disease were considered to be the main causes of death, only some 10 per cent. being attributable to specific diseases. On the available evidence, he considered that it was difficult to assess the importance of wild birds as carriers of disease but thought that primary epizootics were uncommon and that wild birds should not be lightly incriminated in the spread of any disease.

A very useful survey of psittacosis and ornithosis was presented by Meyer (1959) to a Joint Committee of the World Health Organisation and Food and Agriculture Organisation. Without exaggerating the importance of this disease as a public health or agricultural problem he points out that the U.S. Department of Agriculture has taken measures to prevent the spread of ornithosis among poultry and to protect the processor and consumer against infection. Mammalian infections by viruses of the psittacosis group such as ovine pneumonitis and bovine encephalomyelitis are listed.

The incidence of ornithosis among feral pigeons in Paris is of the order of 65 per cent. but the strain appears to have low infectivity for man. The only serious outbreak near the U.K. was that among the women of the Faroe Islands (Rasmussen, 1938) after they had handled fulmar petrels, which were believed to have become infected from eating diseased parrots from South America, thrown overboard after they had died.

In 1952, a Wildlife Disease Association was formed in the United States and is "concerned with the parasites, diseases, physiology and other factors related to health and survival of wild animals, including those in captivity, their effects upon wild populations and their direct and indirect relationships to man" (Herman, 1960). Some centralisation of similar studies in Britain would be of great value to wildlife and game conservation, and might be expected to contribute much information of use to agricultural and public health authorities.

As more land is brought under cultivation or otherwise utilised in remote parts of the world, ecological systems will be increasingly disrupted. For example, campaigns of disease eradication, undertaken with the best intentions, may introduce disease organisms into new environments and biological cycles. Diseases enzootic in wild life may cause, or be associated with, heavy epizootic mortality at times, but can seldom effectively control the wild species. The continued existence of reservoirs of disease calls for strict precautions and prompt treatment where the infection of man and domestic stock is concerned, and the need for much more research into the ecology of diseases in wild life is evident.

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3.—The Role of Wild Life in the Epidemiology of Certain Human Diseases

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THE new and expanding science of epidemiology concerns itself with the whole pattern of disease regardless of its nature or situation. Its primary attention must always be given to communicable disease, but much is being learned by the application of its methods to such chronic and static conditions as heart-disease and cancer. The medical or veterinary epidemiologist relies for much of his data on the work of highly specialised colleagues in such fields as bacteriology, virology, entomology, parasitology, animal ecology, sociology and statistics. Wild animals, from the very fact that they avoid man, have largely escaped the attentions of all these experts and it is true that our knowledge of the infections they carry is far from complete. Fragments of information can be picked up from many diverse sources and only by piecing them together can we hope to appreciate the rôle of wild creatures in the perpetuation of pathogenic micro-organisms in nature.

An impressive list of diseases transmitted between man and vertebrate animals has been produced by the W.H.O. Expert Committee on Zoonoses (1959): it includes 20 bacterial, 7 rickettsial and 31 viral infections. In the following lists only those diseases which may be derived from the wild life reservoir are included.

A glance at these lists is enough to make it obvious that the important reservoirs of infection in wild life are to be found chiefly in rodents, monkeys and birds. These creatures have come to terms with a great many micro-organisms which are potentially pathogenic for man. Both the parasite and the animal host contrive to live together under conditions which ensure that each is perpetrated in nature. If man intrudes into this relationship he may himself become a victim of microbial infection but in many circumstances the chain of events stops short at this point. The human infection is a blind end and the animal parasite is not transferred further from man to man. *Leptospirae*, plague bacilli and other pasteurellae, the psittacosis virus, and the virus of lymphocytic choriomeningitis virus, to name but a few, are rarely transferred directly from man to man. Under special circumstances, however, as for instance when large numbers of micro-organisms are

TABLE I
BACTERIAL DISEASES

Disease	Parasite	Wild animal reservoir
Anthrax ...	*B. anthracis*	Herbivora, wild game
Bacterial food-poisoning	*Salmonella* spp.	Rodents, wild birds
Leptospirosis	*Leptospira* spp.	Rats, mice, voles, hedgehogs, bats, mongooses, bandicoots, foxes, jackals, opossums, skunks, wild cats
Melioidosis ...	*Pseudomonas pseudomallei*	Rodents
Pasteurellosis	*Pasteurella multocida*	Rodents, birds, rabbits
Plague ...	*Pasteurella pestis*	Rats and other rodents
Rat bite fever	*Streptobacillus moniliformis*	Rats
	Spirillum minus	
Relapsing fever	*Borrelia recurrentis*	Small rodents
	Borrelia duttoni	Monkeys
Tularaemia ...	*Pasteurella tularensis*	Rabbits, hares, small rodents

TABLE II
RICKETTSIAL DISEASES

Disease	Parasite	Wild animal reservoir
Murine typhus	*Rickettsia mooseri*	Rats
Scrub typhus...	*Rickettsia tsutsugamushi*	Small rodents
Spotted fever...	*Rickettsia rickettsiae*	Many small rodents, dog, opossum, rabbit, etc.
Q fever ...	*Coxiella burneti*	Birds, rodents, bandicoots

TABLE III
VIRUS DISEASES

Disease	Vector	Wild animal reservoir
B virus encephalitis	None	Monkeys
Lymphocytic choriomeningitis	,,	Mice, monkeys
Newcastle disease	,,	Wild and domestic birds
Psittacosis ...	,,	Psittacines, pigeons, sea-fowl, etc.
Rabies	,,	A variety of mammals, including bats

exhaled and are disseminated in an atmosphere in which people are crowded together, epidemics may occur. Thus bubonic plague may assume pneumonic characteristics and a severe epidemic form.

Some bacteria, however, are able to establish themselves quickly in the human host and to remain in his tissues for prolonged periods. These species spread very readily amongst their new hosts and back again to their original animal source, persisting in either almost indefinitely. Pre-eminent in this type of infection are the types of Salmonellae, over 400 in number, which are to be found in the great majority of mammalian and avian species. Boycott's recent work has shown that reptiles also carry the organism and the pet tortoises imported to this country from the Eastern Mediterranean excrete the organisms. Salmonellae are practically ubiquitous and have often been mistakenly thought to be the cause of a wide variety of diseases (*e.g.*, psittacosis, typhus fever, etc.). They have become established in cattle, pigs, poultry and man as well as in rodents. Rats, mice and guinea-pigs all suffer naturally from infections with *Salm. typhimurium* and *Salm. enteritidis*. The laboratory worker is only too familiar with the epizootic which occurs when these organisms spread in the animal house and destroy most of the stock. *Salm. typhimurium* is the commonest Salmonella type to affect man and was responsible up to 1955 for 44 per cent. of all the reported incidents of food poisoning. It still remains as the most frequent cause, but since 1955 other types of Salmonella are beginning to rival it. (Cockburn, 1960; Taylor, 1960). In epidemiological studies the information about the chain of infection is seldom complete and usually it is impossible to incriminate mice and rats as the direct source; more often the source is found in domestic animals or poultry which may, in their turn, have acquired the infection from rodents. Since 7.3 per cent. of rats have been found to harbour either *Salm. typhimurium or Salm. enteritidis* they

TABLE IV
ARTHROPOD BORNE VIRUS INFECTIONS

Group A.	Equine encephalomyelitis: Eastern, Western, Venezuelan, Mayaro, Middleburg, Sindbis, Semliki Forest	Mosquito	Wild birds
Group B			
Subgroup 1	Dengue 1 & 2	Mosquito	Wild birds
Subgroup 2	St. Louis, Japanese B, Murray Valley, West Nile	Mosquito	Wild birds
Subgroup 3	Russian Haemorrhagic Complex, Russian spring summer, Louping ill, Omsk Fever, Kayasanur Forest Disease	Tick	Wild birds, Small Rodents, Monkeys
Subgroup 4	Yellow Fever, Uganda S	Mosquito	Monkeys
Group C.	Apeu, Marituba, Oriboca	Mosquito	? Monkeys
Unclassified	Rift Valley Fever	Mosquito	Rodents and monkeys
	Sandfly Fever	Phlebotomus	?
	Colorado Tick Fever	Tick	Rabbits and rodents
	Crimean Haemorrhagic Fever	Tick	Rabbits and rodents

must constitute an important and continuing danger to man and animals and an almost permanent reservoir of disease.

The folly of the deliberate introduction of certain bizarre types of Salmonellae as "poisons" into rodent populations has been demonstrated on countless occasions when epidemics of gastro-enteritis in man due to the self-same organism have resulted.

There are other agents, notably the Rickettsiae and the group of arthropod borne (Arbor) viruses which, except under unusual circumstances, are unable to spread from vertebrate to vertebrate without the aid of an arthropod vector. To understand the epidemiology of this group of infections is an exacting task because all the factors influencing the inter-relationships between the vertebrate host, the parasite and the arthropod must be equated in terms of quantitative ecology. More than one vertebrate host and more than one arthropod vector may well be involved in any one assemblage and each may be profoundly influenced by geographical and climatic conditions, by vegetation, and by man's intervention. The word *biocenose* has come into use to convey the concept of the ecological factors assembled in comprehending the natural history of arbor virus infections.

In many biocenoses the virus has adapted itself so well that it circulates in the blood stream of the

vertebrate host and infects the biting arthropod without harming either; examples of this would include birds and mosquitoes with the eastern equine encephalomyelitis virus and monkeys and mosquitoes with the yellow fever virus. The long-term maintenance of these infections in vertebrates requires the transovarial transmission of the virus in the arthropod vector. Thus the vector is itself a reservoir of infection and fresh generations carry the virus on from one season to the next. Indeed many hold that the arthropod was the original host of the parasites which only adapted themselves to animals at a later stage in their evolution. Mosquitoes, ticks, mites and lice are all known vectors of this type and each may acquire a variety of viruses from differing hosts. Factors such as the amount of virus circulating in the vertebrate host, the amount of virus ingested by the arthropod, and the size of the infecting dose injected into the new susceptible host are all of paramount importance in the establishment and maintenance of infection.

Man is probably nothing more than an incidental host in arbor virus biocenoses. Seldom, if ever, does he become a maintaining host for arbor viruses, although in the past yellow fever was maintained in urban populations by mosquito transference from man to man. The same may be said of horses which are only incidentally infected with the equine encephalomyelitis viruses transferred to them by mosquitoes from the reservoir in birds. Of the interesting reservoirs of infection in wild life it will be possible to select only a few from each of the three main sources for further consideration.

Mice and Rats

Lymphocytic choriomeningitis

The common clinical form of this infection in man is that of a severe meningo-encephalitis—a picture which is liable to be mistaken for tuberculous meningitis until its benign course becomes certain. The sources of infection are the nasal secretions, urine and faeces of mice and the most probable route by which the virus is acquired is inhalation. Although relatively uncommon in Great Britain the disease may elsewhere assume epidemic proportions when mice abound and when warm, dry, dusty conditions occur. Adair *et al.* (1953) found in the U.S.A. that 9 per cent. of 854 sporadic cases of aseptic meningitis were due to L.C.M. virus.

The great interest in this infection lies in the enzootic nature of the reservoir in mice. In one colony of mice (Traub, 1936 a and b) a fully enzootic condition was established and maintained for many years. Although most of the mice in the colony were apparently healthy their tissues contained large amounts of the L.C.M. virus. The infection persisted throughout life and was regularly transmitted to the foetus *in utero*. When congenitally infected mice were examined after birth no specific antibodies for the L.C.M. virus could be detected in their blood. Here an almost ideal compromise had been achieved between the host and the virus; both were able to continue life without harm to each other and even the foetal tissues remained undamaged. Burnet (1959) has suggested that this phenomenon is an example of a viral antigen being introduced sufficiently early in intrauterine life for the host embryo to accept it as a "self" constituent to which it makes no antibody response. Other examples of this immune tolerance may include some of the tumour-producing viruses, notably the Bittner agent which in company with certain factors in the genetic constitution and a suitable hormonal status gives rise to spontaneous mammary carcinomata in mice.

Such phenomena of immune tolerance may be more frequent than is at present realised and might exist in other reservoirs of infection where host and parasite live easily together. Closer investigations of rodent populations, with careful surveys of antibody levels and the incidence of pathogens, would be of the greatest interest in this respect.

Leptospirosis

For many years rats, field mice and dogs have been known as the source of leptospiral infection in man; over 30 years ago in a survey of the rodent population in South-East Scotland Buchanan (1927) estimated that 36.7 per cent. of rats carried *Leptospira icterohaemorrhagiae*. These micro-organisms colonise the renal tubules and are discharged in very large numbers in the urine; they remain viable under favourable conditions for many hours and by virtue of their active motility are able to enter new hosts through mucous membranes and small abrasions in the skin.

During recent years, however, at least 34 leptospiral serotypes have been characterised, 25 of them since 1954. Many new hosts of leptospirae have been described (Babudieri, 1958) and bats, bandicoots, mongooses, shrews, jackals, foxes, opossums, skunks and wild cats are all known reservoirs of infection. In the U.S.A. in a survey of 820 mammals of 14 different species 5.4 per cent. were proved to harbour leptospirae of one type or another. *L. canicola*, originally regarded as a canine pathogen, is now known to infect cattle, pigs, swine and jackals. (Alston & Broom, 1958.)

In this country we had imagined we had only 2 pathogenic leptospirae, *L. icterohaemorrhagiae* and *L. canicola*, but it now appears that others exist in wild life, and Broom and Coghlan (1958) isolated *L. ballum* from the kidneys of wood mice, voles and bank voles; the same authors (1960) also recovered *L. bratislava* from a hedgehog. It is interesting to note that of 15 mice harbouring leptospirae only 3 had specific antibodies in their serum for the strain carried; the hedgehog also lacked the type specific antibody. A possible explanation of Broom and Coghlan's findings is that these leptospirae are of low virulence for their hosts and that like the L.C.M. virus they are unable to harm the embryos which accept them as "self" so that there is no stimulus for antibody production. To date there are no records of human infection with these two leptospiral strains in this country although they are known to be pathogenic for man. It is, no doubt, only a matter of time before the routine serological

screening of human sera reveals cases of infection in Great Britain.

Rat-bite Fever

Although this infection is rare in man in this country it presents a hazard which may threaten life. The infection is due to *Spirillum minus* or rather more frequently to *Streptobacillus moniliformis* which is a natural parasite of the rat. The latter is found as a commensal in the upper respiratory tract of up to 30 per cent. of both wild and laboratory animals. Only recently an animal handler in Edinburgh developed a swinging temperature some 3 weeks after a rat bite; embolic phenomena and cardiac insufficiency indicated the diagnosis of acute ulcerative endocarditis and *S. moniliformis* was isolated from the blood a few hours before death.

Monkeys

Virus B

This agent is a natural parasite of monkeys. In a colony of normal monkeys 27 per cent. of the animals were found to have antibodies to virus B (Krech & Lewis, 1954) and the incidence has been known to rise to 75 per cent. when the animals have been housed together for 6 weeks or more (Keeble *et al.*, 1958). These authors described an outbreak of stomatitis due to the virus with an incidence of 2.3 per cent. amongst 1,400 rhesus monkeys. There was histological evidence of involvement of the central nervous system in 25 per cent. of the animals even when there were no clinical signs of a lesion. The virus has also been isolated from the nervous system of apparently normal monkeys and from monkey tissue cultures used to prepare pools of virus for poliomyelitis vaccine production (Wood & Shimada, 1954; Melnick & Banker, 1954). The contamination rate on virus pools of this type was 1 per cent. (6 of 650 pools).

In man infection is usually the result of a bite from an infected monkey although there are cases recorded in which the patient was infected by spilt tissue culture fluid. The local lesion becomes red and swollen within about 2 days and around the purulent lesion are a number of small vesicles. Somewhere between the tenth and twentieth days after the bite an acute encephalomyelitis results with early coma and death. Occasionally the disease takes the form of an ascending myelitis with death due to respiratory paralysis. The human disease is almost always fatal and there is only one recorded instance in the literature of a patient recovering.

An examination of the epidemiological features of B virus infections in monkeys reveals close similarities to those of herpes simplex in man. Both viruses in their respective hosts exist for long periods in a latent form involving as many as 75 per cent. of the population without causing more than minor or trivial recurrent lesions. When these viruses infect the susceptible host for the first time they are able to give rise to an apthous stomatitis. The pseudorabies virus is as widespread in swine in the U.S.A. as is the herpes simplex in man. On transference to unaccustomed hosts for the first time, especially to rabbits and small rodents, all 3 of these viruses assume highly invasive neurotropic qualities and give rise to a rapid and uniformly fatal encephalitis.

Virus B has a close antigenic relationship to the herpes simplex virus and a remote one to the pseudorabies virus (Burnet *et al.*, 1939). Human gammaglobulin in the U.S.A. and serum from "normal" people in Bombay have strong neutralising properties for both virus B and the herpes simplex virus. It seems that virus B has the more complete antigenic structure because an antiserum to it neutralises herpes simplex as well or better than it neutralises itself. A herpes simplex antiserum has but little power to neutralise virus B.

Thus the evidence suggests strongly that these 3 viruses spring from a common origin and that each has become highly specialised for its own host species, herpes simplex for man, virus B for monkeys and the pseudorabies virus for swine. It is for these reasons that they have been renamed *Herpesvirus hominis*, *Herpesvirus simiae*, and *Herpesvirus suis*.

Foamy Agents

The development of the salk vaccine against poliomyelitis has required the use of huge numbers of monkeys to provide cells for the progagation of the viruses and for use in the elaborate safety tests which are required before the finished product can be put into use. Monkey tissue is also used extensively in medical diagnostic work and in fundamental virological research. The contamination of simian tissues with indigenous commensal monkey viruses has bedevilled the virologist working in this field and still is responsible for the discarding of tissue cultures on a large scale. These viruses must have been responsible for the needless slaughter of many thousands of monkeys and for much financial loss. In 1957 Hull and Minner described the cytopathic effect and some of the more important properties of 16 different strains of these simian viruses. "Foamy agents" are given their name from the peculiarly characteristic foaming that they produce in tissue culture cells; there is a marked vacuolation in the cell cytoplasm giving a lace-like or bubbly appearance. The effect often obscures entirely the specific cytopathic effect of the virus under cultivation and may completely vitiate many hours of patient and highly skilled work. As far as is known, foamy agents exist in a latent form in the living monkey where their activity is largely held in check by the animals' defence mechanisms. When the cells are freed from these influences by the trypsinisation processes of tissue culture, these viruses are free to multiply and to cause the foaming effect.

During vaccine safety testing these workers found that 35 per cent. of pools made from 10 to 20 monkey kidneys contained one or other of these viruses and that even when 16 pools were prepared from only two kidneys 22 per cent. were contaminated. Although the incidence of these viruses is subject to seasonal variation and can be, to some extent, controlled by careful isolation of the animals much loss of time and money still results.

Ruckle (1958) found a foamy agent in 57 per cent. of 99 monkey kidney cell batches and showed that a second agent which he refers to as monkey-intra-nuclear inclusion agent (MINIA) was similarly unmasked in 17 per cent. of trypsinised monkey kidneys. MINIA produced precisely the same cytopathic effect in the cells as does the measles virus. Cross neutralisation and cross complement fixation tests showed that MINIA and the measles virus are so closely related antigenically as to be indistinguishable. MINIA in its cytopathogenic effects and immunologically was, however, quite distinct from foamy agents.

Some foamy agents are of faecal origin and are associated with diarrhoea in the monkey; they are very similar to the ECHO viruses in man. Apart from this, however, there is but scanty information available about their pathogenicity for man or monkeys. There seems to be but little crossing in serum neutralisation tests between the strains. One strain SV_4 is, however, frequently inhibited by heterologus antisera and by normal sera so that poliovirus antisera may prevent its cytopathogenic activity.

It is obvious that these viruses constitute a potential danger to man either in the laboratory or when he is the recipient of vaccines prepared in monkey kidney tissue cultures. Much work remains to be done in studying the properties of this group of viruses and in controlling their spread in monkey colonies. One advance that is being pursued is the development of antisera to foamy agents for inclusion in tissue culture media.

Wild Birds

Psittacosis-ornithosis. Although psittacine birds were the first source of infection to be recognised for man and although the majority of human infections to be reported have occurred in handlers and owners of these species many other birds are now known to harbour the virus. Many inapparent infections occur in turkeys, ducks and pigeons, while sparrows and starlings also frequently carry the virus. Free-flying pigeons and sparrows in large towns and cities although very numerous seldom, however, come close enough to the individual to be able to transfer the virus to man and thus they do not constitute a major hazard to public health. Less than 1 per cent. of cases of viral pneumonia in man are due to infection with this group of viruses.

Newcastle Disease. Disastrous epizootics of fowl pest in this country have repeatedly been caused by the Newcastle virus, and cases have occurred in man, chiefly in laboratory workers. The primary source of the infection is usually the domestic fowl or imported poultry meat. Chickens, turkeys, guinea fowls, and peacocks are all known to be infected but wild birds such as starlings, ospreys, gannets and cormorants are also well recognised as sources of infection. Of particular interest in this respect are the outbreaks that occurred in the Western Isles of Scotland in 1949-51 when MacPherson (1956) was able to trace the origin of multiple isolated outbreaks to the crofters' practice of shooting cormorants and, after removing the breast meat for human consumption, casting the carcase on the manure heap to which free ranging poultry had ready access. A considerable proportion of cormorants shot by MacPherson off the coasts of Lewis and Harris showed virological evidence of Newcastle disease.

Arthropod-borne encephalitides. Of the very large number of viral encephalitides 2 groups are of particular interest; the better studied includes the Eastern and Western equine encephalomyelitis viruses and the virus of St. Louis encephalitis in the U.S.A., while the second group comprises the tick-borne complex of haemorrhagic diseases which are of great importance in Central Europe at the present time.

The main reservoir of the equine encephalomyelitis viruses is in the wild birds; the Eastern strain has been recovered from the tissues of catbirds, hermit thrushes and cardinals, and the Western from loggerhead shrikes, cardinals, and Carolina chicadees (Kissling, 1955). Culicine mosquitoes, which are primarily bird feeders, transmit these viruses to a wide variety of other vertebrate hosts. Their perpetuation in nature depends on maintenance in the wild bird or successful establishment in domestic poultry. When transferred to man, the horse, domestic animals or to some avian species such as the duck the infection cycle comes to a dead end and the virus is lost.

When the virus successfully parasitises a new vertebrate host, provided that a sufficient amount of it circulates in the bloodstream, other vectors as well as the original one may ingest the agent and transfer it to secondary vertebrate host species. Thus more than one vector and more than one vertebrate host may participate. The persistence of the virus in the vector with its transovarian transmission implies an arthropod reservoir of infection which can continue throughout hibernation. The migration of birds, often carrying their own parasites with them, ensures the wide dissemination of the viral encephalides. On arrival at their new location the viruses by variation and mutation are able to adapt themselves to fresh conditions and to set up new biocenoses.

The tick-borne complex of encephalitides provides examples of some of these processes. Although the only member of this group in Great Britain, louping-ill, seems mostly confined within the tick to sheep infection cycle, the virus of Russian Spring-Summer encephalitis which is closely related antigenically and transmitted by the same tick *Ixodes ricinus*, is able to establish itself in the goat. The virus is excreted in the milk and from this source is able to infect man causing a moderately severe meningo-encephalitis with minor pareses. In the past 10 years tick-borne encephalitis has been described clinically and demonstrated virologically repeatedly in Czechoslovakia, the Soviet Union, Poland (Slonim, 1961) and a number of other central European countries.

The causative virus of Omsk fever is antigenically related to the Russian Spring-Summer virus but is transmitted by a different species of tick *Dermacentor pictus* and gives rise to a much graver infection in man with haemorrhagic manifestations. A disease of this character has appeared recently in Mysore

State in India where it is known as Kyasanur Forest fever. The virus is established in the monkey population amongst which it is transmitted by the tick *Haemaphysalis spinigera*. It seems reasonable to postulate that the appearance of this disease in a new and far distant locality has followed the carrying of virus-infected ticks by birds migrating southwards from the Soviet Union.

Conclusions

In looking back at the investigations of zoonoses during the last decade it can be said that attention has been focused primarily on domestic animals almost to the exclusion of wild life. Experience with malaria and yellow fever has led to too great a preoccupation with arthropod vectors to the exclusion of a proper realisation of the natural reservoir of infection in wild vertebrate hosts. It is of the greatest importance that we give full consideration to all the intricate inter-relationships in the natural history of these diseases if we are to achieve our ambitions of being able to control these diseases in man and animals.

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The Speakers' Introduction

The Chairman, Dr. W. S. Gordon, said that the first paper to be presented would be that by Dr. A. McDiarmid, a Principal Scientific Officer at the Agricultural Research Council's field station at Compton; the second paper would be presented by Mr. H. V. Thompson, a Principal Scientific Officer at the Infestation Control Laboratory near Guildford, the third paper would be presented by Dr. R. H. A. Swain, Reader in Virology at the University of Edinburgh, and Mr. A. R. Jennings, a lecturer in Pathology at the Veterinary School in Cambridge, would open the discussion.

Dr. A. McDiarmid, in presenting his paper, said that the symposium was of an unusual nature, and at first sight apparently somewhat remote from the day-to-day problems of the veterinary surgeon and, for that matter, the laboratory worker as well. Instead of following the paper in detail, he had selected a few points of general interest to try to give some idea of the importance of the problem, not only to veterinary surgeons but also to the general public.

Dr. McDiarmid showed a slide enumerating certain headings. Dealing first with economic cosiderations, he said there was no doubt that myxomatosis was of considerable economic importance. In 1953 it was stated that the money saved to agriculture and forestry by that one disease was probably in the region of 3 or 4 times the amount which had come in from the sale of rabbits. Further, shooting rights on some estates and farms were very expensive, and if the game population was healthy, there was a good chance of letting the shooting at a considerable price. In some areas this could be as much as 10s. per acre.

To move to the next heading "Reservoirs of Infection" and "Silent Hosts," it was well known that wild animals were reservoirs for important diseases. The phrase "silent host" had come into being recently, and it meant a situation where a wild animal was harbouring a parasite or virus which had no apparent effect on it, but which could, of course, infect other stock. An interesting feature was that many of those organisms and the hosts got along so well together that no antibody was formed. This was somewhat disturbing, as previously it was felt that a good way to find out about diseases in wild life would be to look for antibodies. It now appeared as though certain diseases could exist in wild animals without any evidence of antibodies.

Turning next to "Specific Wild Life Infections," certain populations had their own diseases. For example, there was the acid-fast organism which Dr. Wells did so much work with, and the mycotic infection of moles which had not so far appeared in domestic stock or in man. As to the actual effect on population, one need only mention myxomatosis.

With regard to detectors of abnormal conditions, one immediately thought of radioactivity. There was evidence to show that certain birds could carry a considerable quantity of radioactivity and be affected by it. A medical friend of his noticed that a redshank had not altered its plumage at the time of the year when it should have altered it, and he sent it for examination. It was found to be radioactive.

To move on to the contamination of water supplies, the best example of such infection was probably tularaemia in the United States. Some mountain streams which might have appeared to be of good quality were in fact affected by carcases of animals dying from this disease. Then as one moved on to food, the obvious causes of contamination were the salmonella group. There were of course other possibilities. Pseudotuberculosis was common in wild species, and one wondered whether there might be some risk associated with fresh salad crops in that they might be contaminated by wild pigeons in which the disease was common.

The next heading was meat inspection. There was not much meat inspection done in connexion with game and wild birds; but obviously more attention should be paid to that particular subject.

As to antigens, a very good antigen had been prepared from the vole bacillus, which had been used for the prevention of tuberculosis in man and also in animals; it was a very good illustration of one of the useful side effects of research in that field. In Sweden some workers had used strains of *Pasteurella* isolated from hares for the immunisation of guinea-pigs. In Britain, he had found to the contrary, that strains of *Pasteurella* from wild life were invariably fatal to guinea-pigs.

As to the varying characters of infective agents, it was interesting from a bacteriological angle because he had found that many of the strains of organisms which were obtained from wild hosts differed in character from the types obtained from domestic stock, and he wondered whether the basic classification of strains might need alter-

ing, because, after all, those organisms had probably been in the wild hosts far longer than in any domestic animals.

As to the question of disease eradication schemes, it was dangerous to go ahead with an eradication scheme without knowing something about the possibility of other hosts for the type of infection being dealt with. This had already cropped up in the United States where an attempted control programme for brucellosis was interrupted by the fact that *Brucella* infection was present in elk living in proximity to the domestic stock.

As to potential experimental animals, there was a possibility that hedgehogs and shrews and other small wild mammals with their own specific helminth infections might be useful for testing therapeutic substances or immunological procedures. They had, for example, their own lung typical worm infection.

With regard to epidemiological studies, he did not think that disease should be studied without looking at the picture as a whole. So often it was found that species of wild life were the principal hosts. If animals were to be confined in national parks and other refuges, it was necessary to know something about the diseases to which they were subject, otherwise sooner or later one would be faced with a very difficult problem.

With reference to migration and the introduction of disease, there was good evidence that this did in fact happen. There was some useful information on the trans-equatorial transmission of some of the tropical fevers to Australia.

Coming to aesthetic and recreational values, there was no doubt that myxomatosis caused a great deal of public feeling. It was not pleasant to see masses of dead rabbits. A similar process had been gone through again recently as a result of toxic chemicals. It caused considerable mortality, and since 1956 many people living in the country had been appalled at the deaths of many wild birds of different species caused through the indiscriminate use of toxic chemicals in agriculture. Farmers had a tendency always to use far more than was in fact required, and probably the amount of poison which had been laid on the land in the last 4 or 5 years was far in excess of what was necessary. However, action had been taken in this matter and an improvement should be seen next spring.

Many people were still interested in country sports, and it would be a pity if an eye were not kept on the disease situation in game birds, because in the countryside shooting was a very important recreation nowadays.

These were some of the reasons why he considered that the problem should have received more attention that it had done in the past.

Mr. H. V. Thompson said that the symposium covered a very wide field and, as far as mammals and birds were concerned, he was aware that he had done no more than scratch the surface; but it was gratifying to see that there were a number of people present who were well qualified to amplify any subjects which he might have touched on.

Fluctuations in the abundance of wild life were considerable and, although disease was one of the causes of mortality, it was only one and not necessarily always a very important one. From the disease point of view wild birds and mammals were interesting in two major aspects. First they provided reservoirs of infection which might pass to domestic animals and man and, secondly, they could act as vectors of disease.

The symposium seemed to come at a very appropriate time in that there was really world-wide interest in diseases associated with wild life, and one of the latest indications of that was the setting up of the Zoonoses Research Centre in the University of Illinois. More work was needed in that field, particularly in Britain. Compared with some other countries Britain had neglected the field, and what was particularly needed was a focal point to which people could apply for information and where comparative research could be planned. Quite a number of studies had been going on in different parts of the country, and some of the individuals knew each other and knew what was happening; but there was no centre at which that could be brought together. It would be desirable to see more collaborative work between pathologists on the one hand and ecologists on the other. One example was work on foot-and-mouth disease, and the possible rôle that starlings played in the transmission of the disease. This was a subject which could profitably be reopened and studied in more detail. It was known that one or two of the senior ornithologists were interested in the subject, and might contribute new ideas to his work.

Hares could also do with more investigation, particularly in regard to mastitis and brucellosis, and deer from the point of view of bovine tuberculosis, foot-and-mouth disease and brucellosis. Finally, a number of surveys of disease in wild life, mammals and birds, on a larger scale than had been done hitherto might be undertaken.

Towards the end of his introduction Mr. McDiarmid asked about toxic chemicals. It was something which affected various branches of the Ministry of Agriculture, and in the Infestation Control Laboratory more work was to be done in following up the deaths from toxic chemicals during the next year or two. It was hoped to engage additional qualified staff to carry out the work. Some sort of survey centre was really required. The chemical work could probably best be done by the Ministry of Agriculture together with a certain amount of ornithological work. Other studies were going on in a number of other organisations. Pathological investigations should be integrated with the toxicological and ecological surveys.

Dr. R. H. A. Swain said that his concern was to draw attention to the human infections which were derived from wild animals. That was no easy task because neither the physician nor the medical laboratory worker had turned his attention to wild life, and had always been preoccupied with the patient himself and the diagnosis of his disease. Thus for many years yellow fever was thought of as a man—mosquito—man chain of infection, and it was only recently that it had been realised the disease in its natural form, sylvatic or jungle yellow fever, was a disease of monkeys often living in the canopy of the jungle and usually transmitted by tree dwelling mosquitoes of a quite different species from those that used to transmit human yellow fever in its urban form.

It would be profitable to look at the lists of diseases which could be picked up by man from animals. It was a frightening list when one considered the number listed by the World Health Organisation expert committee on Zoonoses. There were more than 60 such diseases which could affect man, and even when the list was cut down to those derived from wild life, it was still a considerable list.

Dr. Swain showed a slide enumerating the diseases transmitted to man bacterially, which included salmonellosis and leptospirosis, and others which had been dealt with by other speakers. A second slide showed the rickettsial diseases, particularly the 3 types of human typhus and Q fever, which presented a problem in this country. The third slide showed some important virus diseases, including B virus encephalitis, lymphocytic choriomeningitis and Newcastle disease.

The fourth slide showed a much abbreviated list of the arbor viruses which formed a group of over 100 human infections in the United States and in the tropics, about which knowledge was increasing. Rapid advances had followed the new techniques of virus isolation and a determination of antigen structure. Tissue culture, suckling mouse inoculation and H.I. tests had all played a part.

The main wild animal reservoirs of human infection as known at present were: monkeys, birds and rodents. All those creatures had established relationships with a great variety of micro-organisms which were potentially pathogenic for man. Each survived and host and parasite were perpetuated in nature. If man intruded into that relationship he might himself become a victim of microbial infection, but usually the chain of events stopped short there, with the exception of salmonella.

Considering first the simian host, virus B was a natural parasite of monkeys. In a colony of normal monkeys 27 per cent. of the animals were found to have antibodies to virus B, and the incidence had been known to rise to 75 per cent. when the animals had been housed together for 6 weeks or more. Clinically in the monkey the disease was characterised by an apthous stomatitis, and in one instance

an incidence of 2.3 per cent. was found amongst 1,400 rhesus monkeys. There was histological evidence of involvement of the central nervous system in 25 per cent. of the animals even when there were no clinical signs of a lesion. The virus had also been isolated from the nervous system of apparently normal monkeys and from monkey tissue cultures used to prepare pools of virus for poliomyelitis vaccine production. The contamination rate in virus pools of that type was 1 per cent. or 6 of 650 pools. In man the infection was usually the result of a bite from an infected monkey, although there was one case recorded in which the patient was infected by spilt tissue culture fluid. The local lesion became red and swollen within about 2 days and around the purulent lesion were a number of small vesicles. Between the 10th and 20th days after the bite, an acute encephalomyelitis resulted with early coma and death. The human disease was almost always fatal and there was only one recorded instance of a patient recovering. Occasionally the disease took the form of an ascending myelitis with death due to respiratory paralysis.

An examination of the epidemiological features of virus B infection in monkeys revealed close similarities to those of *herpes simplex* in man. Both viruses existed for long periods in a latent form in their respective hosts involving as many as 75 per cent. of the population without causing more than minor or trivial recurrent lesions at mucocutaneous borders. When the viruses infected the host for the first time they were able to give rise to an apthous stomatitis. The pseudorabies virus of Aujesky's disease behaved in swine in the United States in that fashion also, and it was as widespread in that country as was *herpes simplex* in man. In this country Burrows in work yet to be published had found that 30.8 per cent. of adult pigs in Northern Ireland had neutralising antibodies. Samples in England, Scotland and Wales showed an incidence of 3.2 per cent., and there was a higher incidence of 6.6 per cent. in West Shropshire and Montgomeryshire.

Those 3 viruses when transferred from their accustomed hosts to others, especially to small rodents, all assumed highly invasive qualities, became neurotropic and gave rise to rapid and fatal encephalitis. All 3 were related antigenically. Virus B would appear to be more complete antigenically because an antiserum to it neutralised *herpes simplex* as well or better than it neutralised itself. A *herpes simplex* antiserum had but little power to neutralise virus B. In other words, it was a one-way cross, and there was a remote relationship to pseudorabies. The 3 viruses were now called *Herpesvirus hominis, Herpesvirus simiae* and *Herpesvirus suis*. Evidence thus suggested that each sprang from a common origin, and each was highly specialised and adapted to its own host—virus B for monkeys, *herpes* for man and pseudorabies for swine.

The development of the Salk vaccine against poliomyelitis had required the use of large numbers of monkeys to provide cells for the propagation of the viruses and for use in the elaborate safety tests which were required before the finished product could be put into use. Monkey tissue was also used extensively in medical diagnostic work and in fundamental virological research. The contamination of simian tissues with indigenous commensal monkey viruses had bedevilled the virologist working in that field and was still responsible for the discarding of tissue cultures on a large scale. In 1957 Hull and Minner described the cytopathic effect and some of the more important properties of 16 different strains of those simian viruses. Foamy agents were given their name from the peculiarly characteristic foaming that they produced in tissue culture cells. There was a marked vacuolation in the cell cytoplasm giving a lace-like or bubbly appearance. As far as was known, foamy agents existed in a latent form in the living monkey where their activity was largely held in check by the animals' defence mechanisms. When the cells were freed from those influences by the trypsinisation processes of tissue culture, those viruses were free to multiply and to cause the foaming effect.

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Some foamy agents were of faecal origin and were associated with diarrhoea in the monkey. They were very similar to the ECHO viruses in man. Apart from that, however, there was but scanty information available about their pathogenicity for man or monkeys. It was obvious that the viruses constituted a potential danger to man either in the laboratory or when he was the recipient of vaccines prepared in monkey kidney tissue cultures. Much work remained to be done in studying the properties of that group of viruses and in controlling their spread in monkey colonies. One advance being pursued was the development of antisera to foamy agents for inclusion in tissue culture media.

Turning now to the second important reservoir, the rodent, since 1954 25 new leptospiral serotypes had been characterised. There were some 34 in all. Bats, bandicoots, mongooses, shrews, voles, jackals, foxes, opossums, racoons, skunks and wild cats were all known reservoirs of infection. In the United States in a survey of 820 mammals of 14 different species 5.4 per cent. were proved to harbour *Leptospirae* of one type or another. It would be surprising if in this country wild life was devoid of infection with *Leptospirae*, yet until 1958 it was imagined that there were only 2 types—*L. icterohaemorrhagiae* and *L. canicola*; it appeared however that others existed in wild life, and Broom and Coghlan in 1958 isolated *L. ballum* from the kidneys of wood mice, voles and bank voles. At the same time *L. bratislava* was recovered from a hedgehog. It was a matter of interest that of 15 mice harbouring *Leptospirae* only 3 had specific antibodies in their serum for the strain carried. The hedgehog also lacked the type specific antibody. A possible explanation was that the *Leptospirae* were of low virulence for their hosts and that like the L.C.M. virus they were unable to harm the embryos which accepted them as "self" so that there was no stimulus for antibody production. To date there were no records of human infection with those 2 leptospiral strains in this country although they were known to be pathogenic for man. It was, no doubt, only a matter of time before the routine serological screening of human sera revealed cases of infection in Great Britain.

With regard to lymphocytic choriomeningitis, the common clinical form of that infection in man was that of a severe meningo-encephalitis. The sources of infection were the nasal secretions, urine and faeces of mice and the most probable route by which the virus was acquired was inhalation. The interest in that infection lay in the enzootic nature of the reservoir in mice. In one colony of mice a fully enzootic condition was established and maintained for many years. Although most of the mice in the colony were apparently healthy, their tissues contained large amounts of the L.C.M. virus. When congenitally infected mice were examined after birth no specific antibodies for the L.C.M. virus could be detected in their blood. An almost ideal compromise had been achieved between the host and the virus. Both were able to continue life without harm to each other and even the foetal tissues remained undamaged. Such phenomena of immune tolerance might be more frequent than was at present realised and might exist in other reservoirs of infection where host and parasite lived easily together. Closer investigations of rodent populations, with careful surveys of antibody levels and the incidence of pathogens would be of the greatest interest in that respect.

To illustrate the third reservoir of infection in birds Dr. Swain showed slides illustrating the infection chains in Eastern and Western encephalomyelitis. Birds were the important natural hosts, but it was not determined whether the species, and if so which, were of primary or secondary importance. The primary vector in sylvan transmission cycle was *Culex tarsalis*. One explanation of the *Culex tarsalis*-bird feeding cycle was that *Culex tarsalis* was

attracted by CO_2. Foliage gave off CO_2 at night when photosynthesis ceased and culicines were attracted to areas where birds were nesting. This might also apply to mammals, for 14 per cent. of the rabbits which were the subject of a survey in Nevada had W.E.E. antibodies. It would be of interest to know whether this also applied to myxomatosis.

Human infections in an area where a given proportion of mosquitoes existed depended on the attack or biting rate for man, which in turn varied with the mosquito population. In a high mosquito population the biting rate for birds diminished and increased for man and domestic animals. If the avian population diminished the biting attack rate for man increased.

When the virus successfully parasitised a new vertebrate host, provided that a sufficient amount of it circulated in the bloodstream, other vectors as well as the original one might ingest the agent and transfer it to secondary vertebrate host species. Thus more than one vector and more than one vertebrate host might participate. The persistence of the virus in the vector with its transovarian transmission implied an arthropod reservoir of infection which could continue throughout hibernation. The migration of birds, often carrying their own parasites with them, ensured the wide dissemination of the viral encephalitis On arrival at their new location the viruses by variation and mutation were able to adapt themselves to fresh conditions and to set up new biocenoses.

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The causative virus of Omsk fever was antigenically related to the Russian spring-summer virus but was transmitted by a different species of tick *Dermacentor pictus* and give rise to a much graver infection in man with haemorrhagic manifestations. A disease of that character had appeared recently in Mysore State in India where it was known as Kyasanur Forest fever. The virus was established in the monkey population amongst which it was transmitted by the tick *Haemaphysalis spinigera*. It seemed reasonable to postulate that the appearance of that disease in a new and far distant locality had followed the carrying of virus-infected ticks by birds migrating southwards from the Soviet Union.

In conclusion Dr. Swain joined with the other speakers in a plea for surveys of the wild life of this country in which careful studies were made to gauge the incidence of pathogenic agents by their isolation, and of serological surveys to discover the immunological status of the animal population. Such work would be of immeasurable value and would draw together in close collaboration the medical and veterinary professions, as well as their ancillary scientists and laboratory workers.

The Opener

Mr. A. R. Jennings, in opening the discussion, first thanked the Provisional Committee for their foresight in arranging the symposium at the Oxford Congress. It was particularly appropriate that the subject should be discussed at "this other place" since it was in Oxford that much of the work on ecology and animal populations had originated.

As had been seen from the admirable contributions already presented, wild life diseases sometimes had far reaching implications, but unfortunately those concerned in Britain had not always appreciated the fact. In recent years there had been an ever-growing awareness of the inter-relationship of animal disease and human health, and that had been largely brought about by a better understanding of what was termed ecology. In the western world many countries devoted very considerable sums of money and employed scientists of many disciplines to investigate the diseases of wild animals and birds. No longer, except perhaps in Great Britain, was such work looked upon as the province of the "curious naturalist." Britain was one of the few countries in which there was no centralisation of activities into wild life diseases. There had been no attempts here to co-ordinate research which had been carried out or which was envisaged for the future. The idea of some central bureau for the collection and dissemination of such information had already been discussed by several individual workers and perhaps as a result of the symposium the idea might become something of a reality.

Each of the three speakers had given a comprehensive introduction to three different aspects of the subject. Dr. McDiarmid had dealt with the veterinary aspects. Dr. Thompson with the ecology of disease and Dr. Swain with the transmissions of disease between wild species and man. He congratulated them on their papers. With such a feast of information it was difficult to know which particular piece of cake to take. Perhaps first a somewhat unpleasant one, indeed, a poisonous one. Dr. McDiarmid had raised the issue of toxic chemicals. Since he wrote his paper there had been signs of a change of opinion amongst the scientific advisers to the Government, but one doubted whether that was a case of cause and effect. Toxic chemicals were of direct concern to the whole community. It was a subject upon which much more research was needed. Since the beginnings of agriculture man had had to contend with various kinds of pests and no one could dispute that they caused vast losses in productivity, equally there could be no doubt that inestimable benefits to human and animal health had followed the use of insecticides. Yet it was foolish to pretend that the use of insecticides and herbicides had not brought about and would not continue to bring about other problems. As Sir Clunies Ross said in another context: "The problems of to-day will be followed by others no less grievous. Their solution will depend upon what we do now." To destroy insects, birds and mammals indiscriminately created rather than solved problems. It was a biological law that if two species of animal living together, one feeding on the other, were destroyed in proportion to their number, then the average number of the prey would increase and the average number of the predator would decrease. Thus the practical result of that was that although there was an immediate reduction in the amount of damage caused by the parasite, there was a period afterwards when the numbers of the parasite would rise rapidly to outstrip the natural predators since the predator increase was dependent upon the population density of the parasite. There were many examples of that kind of disturbance of the host-parasite relationship. Most gardeners would be aware of the resurgence of red spider and aphids on fruit trees after spraying with DDT since the insecticide killed off some 30 natural predators of the red spider. Another example was seen where some species of greenfly were unaffected by DDT but their natural enemies the lacewing flies, the hover flies and the ladybird larvae were killed. It should also be remembered that it was not only insect predators which were killed by insecticides. For instance, up to 25 per cent. of the caterpillar population of coniferous woods might be eaten by various species of tits and one brood of nestling starlings might consume between 16,000 and 25,000 insects. As another example of insect control by birds, it had been calculated that woodpecker control of bark beetles in the Southern United States was the only control likely to be effective without costing more than the value of the timber saved.

Apart from the dramatic effects of acute poisoning of large numbers of birds, there were the often overlooked potential effects of chronic poisoning. He had given examples of that elsewhere and did not propose to deal with the subject in detail, but to remind those present that many of the toxic chemicals were cumulative poisons. Legislation in this country was lagging behind others in

that there was no permissible maximum standard laid down for toxic residues in tissues. To say, as did one Government spokesman in a recent debate, that small doses might produce only "some mild indigestion" was to produce the retort that victims of murder by chronic arsenic poisoning showed only mild indigestion because of the smallness of the dose.

He appealed to the manufacturers of toxic chemicals to divert some of the vast sums spent on advertising to furthering research into the long-term effects of those substances.

There was a very extensive literature on the infectious diseases of wild life and annually the statistics increased. The time was now ripe for research into the comparative aspects of those diseases. Why was it that pigeons and small passerines were so frequently infected by avian pox and what were the relationships of those various poxes? What were the factors which allowed for extensive parasitism in some wild species without apparent ill effects? The wood pigeon was frequently infected with *Haemoproteus* spp. and one researcher had described the presence of gametocytes of several species of *Leucocytozoon* in the blood of 7 species of bird. There was said to be a high incidence of trypanosomes in jackdaws and rooks. Did those parasites occur in domestic birds? Had anyone ever looked for them?

Dr. Swain referred to the value of epidemiological methods in cancer and heart disease, and then went on to discuss at length the importance of the animal reservoirs of disease. Mr. Jennings proposed to say a little more on cardiovascular and neoplastic conditions of non-domesticated animals. The domestic fowl was very susceptible to neoplastic conditions. Indeed 1 in 5 was said to be affected with one form or another. He would not agree with Dr. McDiarmid that neoplasia was rare in wild life; uncommon perhaps but not rare. Why did psittacine birds appear to be more often affected with tumours than others, and why were tumours of the gonads more frequent in these birds than in other animals? Neoplasia was not confined to mammals and birds. He drew attention to a recent paper by Wood and Larson (1961) on hepatic carcinoma in trout. Those workers discovered a very high incidence of malignant hepatic tumours in rainbow trout in the United States and a similar condition had been reported from Italy. A number of important points emerged from that paper. First, it was apparently a relatively new disease with a high incidence and it appeared to be directly related to radical changes in fish management over the last decade. The disease had been seen only in certain trout hatcheries where a particular type of pellet feed had been used. The indications were that the condition was due to a carcinogenic agent. That disease provided the comparative oncologist with a new species of experimental animal and perhaps a new carcinogen. It was not inconceivable also that the disease might have some public health significance since rainbow trout were a popular delicacy.

Cardiovascular disease was second only to cancer in its importance, and was of very direct concern to the busy practitioner. It was very probable that comparative studies on atherosclerosis would shed some light upon the pathogenesis of the human disease and a study of vascular disease in free-living wild creatures might provide the initial clues. The incidence of atherosclerosis in captive wild mammals and birds was said to have increased in recent years and several explanations for that had been propounded. There had been a change also in the type and in the distribution of the lesions in those creatures over the same period of time. A still unsolved riddle lay in the observation that spontaneous atherosclerosis was relatively common in some breeds, whereas it was a rarity in other breeds. The vascular lesions in some strains were nearly identical with the disease in man. Some recent work on that disease suggested that atherosclerosis in the pigeon was not directly related to sex, diet or exercise but rather to genetic factors and to age.

Arterial disease occurred in many species of birds. Most present would be familiar with the dissecting aneurysm of the turkey and it had been long known that birds of the parrot tribe were very prone to arterial disease. Sudden deaths due to vascular accidents were not uncommon in those birds as small-animal practitioners would have noted. The sites chiefly affected were the thoracic aorta, the aortic arch and the coronary vessels.

From comparative studies it had been clearly demonstrated that in many species of mammals and birds there was a deposition of lipids beneath the intima of the aorta and other arteries. That was followed by a laying down of a fibrocellular tissue often with degenerative changes. There was subsequent thrombosis and inco-operation of the thrombus beneath the intima. The end result was partial or complete occlusion of the lumen.

Most of the observations had been made on experimental animals and in captive birds and mammals, but similar conditions occurred in free-living species. For example, in a recent survey 2 per cent. of jackdaws he had examined showed early atherosclerosis of the thoracic aorta. Was it the case that some wild species were more prone to arterial disease than others, and if so what were the reasons? Did seed eating birds more often develop atherosclerosis than insectivorous birds? Did the incidence vary from year to year? There was a very rewarding field of research there in comparative cardiovascular disease and the results would almost certainly shed light upon one of the great killing diseases of man. It was very probable too that studies of wild life might help in an understanding of the so-called stress diseases of man. Dr. Thompson mentioned briefly in his paper the effects of pituitary-adrenal exhaustion as a factor in population control. Ratcliffe (1958) in an excellent summary of the factors involved in the regulation of mammal and bird populations lent strong support to what he called psycho-physiological mechanisms whereby in response to an appreciation of increasing density the fertility or the viability of the individual in a population might be reduced. Jenkins in this country demonstrated that partridge chicks from "high tension" parents had a survival rate of only 1.6 per brood, whereas chicks from "relaxed" parents had a survival rate of 8.6 per brood. Perhaps the results of work on stressor agents and their effects in free-living animals might reduce some of the tensions of everyday life for all.

The General Discussion

The Chairman, in declaring the papers open for discussion, drew attention to an expression of opinion common to all the speakers. Thus, Dr. McDiarmid said: "Undoubtedly, far more attention should be paid to the position of wild life in epidemiology. The only available information accumulated in this country in recent years has resulted from the efforts of a mere handful of individuals engaged on other duties and investigating the problem in a part-time capacity."

Dr. Thompson's paper contained the statement: "In 1952 a Wild-life Disease Association was formed in the United States and is 'concerned with the parasites, diseases, physiology and other factors related to health and survival of wild animals, including those in captivity, their effects upon wild populations and their direct and indirect relationships to man.' Some centralisation of similar studies in Britain would be of great value to wild-life and game conservation, and might be expected to contribute much information of use to agricultural and public health authorities."

Dr. Swain, in his final remarks, said, "It is of the greatest importance that we give full consideration to all the intricate inter-relationships in the natural history of these diseases if we are to achieve our ambitions of being able to control these diseases in man and animals."

Mr. Jennings had expressed a similar view and it was perhaps appropriate to put to the meeting that those experienced in the study of diseases in wild life appreciated the need for more opportunity and better organised facilities for such work, because the studies they had made so far were, to a large extent, very much a sideline of their other activities.

Sir John Ritchie (The Chief Veterinary Officer, Ministry of Agriculture) said he had been a little disappointed in the

papers and in the discussion so far. He entirely agreed that more attention should be given to the study of disease in wild life and its association with animal diseases generally. He thought the case, however, had been overstated and a great deal of matter mentioned in the papers might wrongly be taken to apply to this country. If one looked, for example, at Dr. Swain's tables extracted from the list of zoonoses which the World Health Organisation Expert Committee had compiled, it was observed that in Table I only the second and third items were important in this country—food poisoning and leptospirosis, in Table II there was Q fever and in Table III Newcastle disease and psittacosis.

It had been asked whether it was still possible that bats in this country might be carrying the rabies virus, but since the country had been completely free of the disease for 40 years, it seemed unlikely that there was a reservoir in bats which might come to affect other species.

In so far as Newcastle disease was concerned, it was a little unfortunate that wild birds should be listed as a reservoir of infection, and particularly in reference to the coastal areas of Scotland and Northern Ireland. It was perfectly true that there was good evidence that birds had been the source of the spread of infection in these areas. However, the holdings on which domestic poultry had been affected had been completely repopulated in 1949 and 1950 and the flocks had never become infected since then. It did not, therefore, seem likely that wild birds continued to be a reservoir of infection in their vicinity.

Dr. McDiarmid had mentioned the vole bacillus as having been used for the control of tuberculosis in this country. He did not know of the use of this organism other than experimentally for animals in this country.

In foot-and-mouth disease hedgehogs had been mentioned and the possibility that red deer might become involved. There was no doubt that these animals could become involved in the infection, but with the policy followed in this country it was unlikely that they would become a continuing source of infection. Hedgehogs had been recorded as having become infected on one occasion and it was clear enough that they had picked up their infection from cattle originally and served as a link between outbreaks for a period. This was a similar picture to that which occasionally arose when, for example, sheep became involved in the disease and the condition was undiagnosed for a period. It was always necessary to guard against the possibility that deer should become involved in outbreaks of foot-and-mouth disease in this country. Generally speaking, however, it was a question of these wild animals picking up infection from infected domestic stock. Sir John fully appreciated the importance of the relationship between domestic and wild animals in the control of animal diseases but that we should be careful not to overstate the case.

Mr. D. G. Earnshaw (Dublin) said he had some experience in the field under discussion, and he was rather disappointed that no mention was made of African horse sickness. Two years ago when he was V.I.O. in Northern Nigeria, there were reports of large numbers of donkeys and horses being infected at some time previously with a disease. The disease appeared in cycles of 3 or 4 years, and a great many animals, particularly donkeys, were wiped out. He saw one or two clinical cases, and the original thought was that they had some form of biliary fever. The suggestion was made later by the Chief Veterinary Research Officer that it might be African horse sickness which had not hitherto been identified in Nigeria. After a great deal of difficulty serum samples were obtained from various villages where the disease had broken out, and they were sent to Onderstepoort (South Africa) where antibodies of A.H.S. were found. He did not know what happened to that report.

Sir John Ritchie contended that most of the diseases applied to places abroad. It should be remembered that the whole situation was extremely intricate and complex, and on a small scale there could be a population of animals which were not regarded as native to this country coming in and setting up a population. The coypu in East Anglia might be one of these situations. There was always a possibility nowadays with better communcations that some exotic diseases could extend to this country.

In his reference to rat-bite fever Dr. Swain gave some interesting information. Was the domestic cat affected by the bacilli of rat-bite fever and, if so, could it transmit them to the human being? From experience gained in clinical practice it occurred to him that when one found cats with respiratory trouble, very often it was found that someone in the household was also suffering from some kind of respiratory trouble. He did not know whether there was any connexion, but the matter could be investigated.

With regard to medical veterinary co-operation, probably everybody would agree that the veterinary surgeon ought to play more part in the subject under discussion, and not leave it to the amateur naturalist. That was particularly important in the tropical countries, but as far as one knew, in general, game departments were rather divorced from veterinary departments.

Mr. W. J. Herbert (Edinburgh) recalled that a year ago he signed some certificates for horses in Northern Nigeria which were taken round the West Coast of Africa, shipped to France and were then imported into England. The Ministry caught up quickly with them, and the animals were kept in quarantine for a while and were later moved to the continent. He was not aware at that time that African horse sickness had ever been found in Northern Nigeria or West Africa, but it was at the time when African horse sickness was a great worry. It was important not to be so parochial as Sir John Ritchie appeared to be about diseases. Any of them might turn up at any time for a number of reasons.

Sir John Ritchie interposed to say that he was confining himself to the title of the paper, and not trying to be parochial.

Mr. S. A. Keeble (Greenford) referred to virus B infection of monkeys, and said that in the past few years he had considerable experience of that condition. Of the fatal cases which had been reported in the last 10 years, the majority had been in animal attendants, but there had also been a king and a veterinary surgeon! In his original paper it was reported that 1,400 monkeys had been examined and 2.4 per cent. had been found to be infected. That was followed up when 14,000 monkeys were examined and the same percentage were found to be infected. That was not examining monkeys every day, they were examined on one occasion only. Therefore at any one time there were on average 2 per cent. of infected monkeys in the colony. They reached this country 6 weeks after capture in the jungle. On one occasion monkeys coming into the country were examined on the day they arrived and 2 out of 66 had the condition. The practising veterinary surgeon might be presented either with a pet monkey or one in a zoo which had the condition, and he should be very careful how he handled it. It was not only a case of infection by a bite or scratch from the monkey. An aerosol of virus could also cause it, for instance from a monkey which was coughing or sneezing.

It was found on histological examination that animals which survived had normal adrenals whereas adrenal necrosis was a marked feature of the fatal infection. Since virus B and pseudorabies are both members of the *herpes* group of viruses he appealed to anyone with any information regarding the effect of pseudorabies on adrenals of cattle and pigs either to publish it or let him have some of the information or specimens so that it might be possible to tie the two up.

Mr. R. S. T. Bowden (Canine Health Centre, Kennett) supported all the speakers who had advocated something in the nature of a central laboratory. He was associated with some of the work in toxic chemicals, and the question which was constantly asked was "What percentage of birds have you had analysed?" No one owned wild birds or animals, and those who were interested in the subject had had few laboratories to whom to refer those matters.

He was sorry that nothing was said about foxes. The light which had recently been put on wild life had done more than anything to bring together the hunting man and the shooting man. Foxes were a very interesting study.

As to the question of a parochial outlook, those who

had worked in the tropics knew that the diseases could turn up in this country, and those with experience abroad had got together with the medical research people more than had been the case in this country. It was long overdue here.

Dr. A. O. Betts (Cambridge) said that Sir John Ritchie had remarked that monkey viruses were not of particular importance to man in this country, but in one respect they were, now that so many of us were inoculated with poliomyelitis vaccines produced in monkey kidney tissue cultures.

Dr. Swain mentioned the occurrence of both "foamy agents" and B virus of monkeys in tissue cultures used for vaccine production. With the Salk vaccine, a formalin-inactivated one, that might not be of particular importance; but the situation was very different when the Sabin oral vaccine, a living attenuated vaccine, was used.

It became apparent at the meeting of the American Society for Microbiology earlier in the year that a large number of people given the oral vaccine had accidentally been infected with "wild" monkey viruses. Although they had developed antibodies to those agents, no clinical symptoms seemed to have occurred. The accidental ingestion of B virus of monkeys might, however, be a much more serious problem: Dr. Swain had quoted a 1 per cent. contamination rate in pooled tissue—culture fluids. There also seemed to be a risk that other monkey viruses as yet unrecognised might get into the vaccine. It would be interesting to have Dr. Swain's comments on the potential risks with vaccines of the Sabin type.

Dr. E. A. Gibson (Norwich) said he wondered whether the question of rodents carrying salmonellae might not have been somewhat overrated. Dr. Swain had made the point that domestic animals and poultry might acquire salmonella infection from rodents. They might on some occasions, but it was only very rarely that it occurred. Certainly in the case of cattle one would not consider infected rats a likely source of infection. Dr. Swain had said that 7.3 per cent. of rats had been found to harbour salmonella infection. Was this an average figure or based on a single survey? The speaker thought it important to distinguish between town rats and those found on farms, because, in his experience, the latter rarely carried salmonellae unless they were in contact with infected farm livestock.

The Replies

Dr. A. McDiarmid, in reply, said that Sir John Ritchie suggested that he had overstated his case. Dr. McDiarmid's view was that if he had overstated his case, Sir John Ritchie had underestimated the importance of the particular subject, because the world had become very small, and it was necessary to give up the idea of thinking in terms of this country's own problems. It was necessary to look farther afield.

The vole bacillus vaccine had been used in the human subject on quite a wide scale, and he knew a number of people who had been vaccinated with vole bacillus in this country. It had also been used in Africa on a large scale. Cattle had been vaccinated with it experimentally in Britain.

As to the question of whether in fact rodents had any importance in the transfer of salmonella to man, it was really a question of contamination of foodstuffs rather than any question of direct infection. Although there had not been a great deal in the literature on it, there were more than 2 or 3 references. There were also a number of personal experiences. Comparatively recently he heard of a rather interesting case where *Salm. typhimurium* infection had appeared in shop assistants in the vicinity of Winchester. It was found that they had acquired the infection through the habit of eating raw oatmeal, and there was a good chance that the oatmeal, in this instance, had been contaminated originally by rodents.

Mr. H. V. Thompson, in reply, said it was fortunate that in Great Britain wild life carried relatively few diseases which affected man and domestic stock. The major examples referred to in the paper were all in the United States, nevertheless, more should be known about the disease picture of wild life in this country.

The question of introduced species was a vexed one. Legislation permitted the prohibition of the introduction of species of animals if it were thought necessary, but there was a natural reluctance to make a general blanket prohibition on mammals and birds which people wished to bring in as pets. Some introduced species might become pests of agriculture, but the legislators' attitude was usually to wait until there seemed a good case for taking action.

On the question of stress, and its effects on animal populations, it was a matter of great regret to him that Dr. Dennis Chitty was no longer in this country but had emigrated to Vancouver, B.C. Nevertheless, Chitty would continue with his work in Canada, where there were vole problems, and he had encouraged several people in this country to undertake similar work. Work on stress in rabbits was started in Australia 3 years ago, and the first results were now being published in *Wildlife Research.*

Dr. R. H. A. Swain, in reply, said that as far as he knew *Streptobacillus moniliformis* had not been recovered from the cat. The association of respiratory disease with pet owners and their cats was common and could be accounted for in one of two ways. One might be that the pneumonia virus was transferred to man by droplet infection, and that particular virus might conceivably cause either pneumonia or respiratory disease in man, or might be associated with cat-scratch fever. The other might be that the pets were infected by human viruses such as the influenza virus derived from their owners.

With regard to the danger of the virus B strain being included in the living attenuated poliomyelitis vaccine, it was a danger which most people were aware of, and which should be more than taken care of by adequate vaccine safety testing.

As to rodents being a reservoir of salmonella infection, he had found it necessary to look round to find a survey of rodent population for salmonella. The one he quoted was perhaps over 20 years old, and was concerned with a survey of rats in Liverpool. It emphasised the fact that there did not seem to be a recent survey of rat population for salmonella or for many of the other infections which rats carried. There might be reservoirs of salmonella in cattle on farms which were transferred back to rats. It worked both ways.

A vote of thanks to the authors, proposed by the Chairman, was carried by acclamation, and the session then terminated.

DEVON FREE OF SWINE FEVER

Members of the Devon Diseases of Animals Committee were told in Exeter that for the first time in about two years the county was free of swine fever.

Mr. F. H. Ellison, the Ministry of Agriculture's Divisionary Veterinary Officer for Devon, said he hoped everyone would co-operate in maintaining this happy state of affairs by boiling all pig swill. If this was done Devon might stay without the disease.

Mr. Ellison also reported that during the quarter ending September 30th there were 9 cases of anthrax, but since there had been a sharp drop and only one case had been confirmed since October 1st.

"Pathogen-free" Pigs for Research and the Practical Control of Pig Diseases

BY

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SUMMARY.—Pigs that are free from pathogens which do not traverse the placenta and are also devoid of circulating antibodies can be produced by removing unborn piglets from the uterus of the sow in a microbiologically sterile manner and rearing them away from possible infections.

Laboratory animals have been obtained in this way for many years but, to date, no entirely satisfactory nomenclature for animals so produced has been devised. The term "gnotobiotics" has been used to describe the general field of investigation and within the field at least three classes of animals need to be considered. Class I comprises animals reared "germ-free," Class II those intended to be free from the natural pathogens of the species, while Class III comprises animals reared free from certain specific micro-organisms considered undesirable. The problem of nomenclature arises from the difficulties inherent in proving conclusively the disease status of the animals of each class.

The term "pathogen-free, colostrum deprived" (PF) has been used for pigs in Class II and "minimal disease" (MD) for those in Class III. In the U.S.A. the term "Specific Pathogen-free" (SPF) is applied to pigs in both classes.

PF pigs have been produced at Cambridge by a hysterectomy procedure followed by removal of the piglets from the uterus in a sterilised operating hood. The piglets so obtained have been reared in stainless-steel, sterilised incubators. Since the work began 4 years ago 72 litters have been obtained and the overall rearing rate has been 83.5 per cent.

PF and MD pigs have been used in this laboratory for the production of tissue cultures to avoid the presence of "wild" viruses, for the investigation of widespread diseases of low pathogenicity, particularly those caused by enteroviruses, and for the study of human adenoviruses. PF and MD pigs are also of considerable value for studies on genetics, nutrition and housing. In addition they can be used for the control of pig diseases on farms. Although it is only just beginning in the U.K., repopulation of farms with SPF pigs is widespread in the U.S.A. The SPF pigs are produced at licensed veterinary centres and are returned at 4 weeks of age to farms which have been emptied of pigs, cleaned, disinfected and left vacant for 4 to 6 weeks. The reduced disease level in SPF pigs on these farms appears to have resulted in appreciably higher performance but factual information is limited. In addition to controls over the veterinary centres there is in the U.S.A. an ambitious certification scheme for the control of SPF pigs on repopulated farms.

There are good prospects of swine repopulation succeeding in this country providing steps are taken to ensure that pigs coming from primary production centres are free from disease and that the status of MD pigs on farms is maintained. It is suggested that the primary production centres should be licensed by the Ministry of Agriculture and subject to regulations similar to those governing the operation of Artificial Insemination Centres and that attempts should be made to formulate, as a matter of urgency, a control scheme for repopulated herds.

THE tendency over the past few years towards more intensive methods of pig husbandry has resulted in a greater awareness of the importance of freedom from disease if maximum production is to be obtained. For highly efficient production it is no longer sufficient for pigs to free from clinically obvious diseases. Freedom from those diseases which only become manifest by their effects on productivity is also becoming necessary.

Research workers have also appreciated to a greater extent than formerly that pigs used for research purposes must be free from as many diseases as possible if extraneous variables in experimental work are to be reduced to a minimum. Animals free from disease are needed for all types of research with pigs, but their value is most obvious in the study of infectious diseases. For work of this kind experimental pigs are required which are known to be free not only from intercurrent infections but also free from natural antibodies, at least against the disease under study.

In theory there is no problem in producing such pigs. The placenta of the sow is of the epitheliochorial type and the foetuses are well protected against infections *in utero*. Moreover they do not receive maternal antibodies by transfer across the placenta. Thus, to obtain pigs that are both free from pathogens which do not traverse the placenta and devoid of antibodies, all that needs to be done is to remove the unborn pigs from the uterus in a microbiologically sterile way and then to rear them away from possible infection so that colostrum is unnecessary. In practice, however, the procedure is somewhat more difficult.

The techniques that my colleagues Dr. Lamont and Mr. Littlewort and I have developed over the past 4 years are based on those originally described in the U.S.A. by Young and Underdahl (1953) and Young, Underdahl and Hinz (1955). Essentially the

* Paper presented to the Annual Congress of the British Veterinary Association in Oxford on Wednesday, September 6th, 1961.

technique consists of removing the piglets from the uterus of the sow by hysterectomy and rearing them in sterilised stainless-steel incubators on a sterilised diet. Hysterectomy is not, however, the only technique for obtaining microbiologically sterile pigs from the uterus and we are now experimenting with other methods.

Terminology

The problem of nomenclature is an extremely difficult one, and is still far from being resolved. No entirely satisfactory terms have yet been suggested. For many years laboratory animals have been produced free from infectious diseases which do not pass the placenta, and similar techniques have been used for domestic animals other than pigs. Thus, any terms finally adopted must obviously be applicable to all species of animals. From the point of view of the absence or presence of disease there is no difference between animals taken sterile from the uterus and their progeny if all these animals are kept in contact in the same environment. Thus the same basic term is applicable to both. There is, however, a difference between animals taken directly from the uterus and their progeny kept in contact in the same environment when the former are of species, such as the pig, in which antibodies are transferred *via* the colostrum and not across the placenta. In such species, animals taken from the uterus are free from gamma-globulin for a time and may be particularly useful for some research purposes. The actual manner in which the unborn animal is removed from the uterus, whether by hysterectomy, hysterotomy or other techniques is unimportant providing the animal is obtained microbiologically sterile. What is important are the steps taken subsequently to maintain freedom from infection.

Reyniers, Trexler, Ervin, Wagner, Luckey and Gordon (1949) suggested the term " gnotobiotics " to indicate the field of investigation concerned with growing living things by themselves or in association with known kinds of micro-organisms. Within this field at least 3 classes of animals need to be considered.

Class I. Those animals which are removed microbiologically sterile from the uterus of the dam and reared under *sterile conditions*, and the normally born, but microbiologically sterile, progeny of such animals reared under *sterile conditions*.

Class II. Animals which are removed microbiologically sterile from the uterus of the dam and reared in *strict isolation* (but not necessarily sterile conditions) on sterilised food in sterilised equipment. These animals are intended to be free from natural pathogens affecting the species but are not necessarily free from other micro-organisms. The class includes also Class I animals which have been deliberately contaminated with pure cultures of non-pathogenic micro-organisms.

Class III. Those animals which are obtained from the uterus microbiologically sterile but which become conventionally contaminated by a " normal " microbial flora except for certain specific micro-organisms considered undesirable. Class III animals are almost always kept in contact with their normally-born progeny so any term used must include the original stock and their progeny. It must be a broad term since it needs to cover animals kept under a variety of degrees of sanitation. Perhaps sub-division of the group is desirable.

The problem of attaching suitable names to the 3 classes results mainly from the difficulties in proving conclusively the status of the various classes of gnotobiotes.

Class I animals are usually referred to as " germ-free." Routine bacteriological tests can be made on the excreta but these cannot, of course, take account of non-bacterial micro-organisms.

The animals in Class II are more difficult to name. The term " pathogen-free " has been used for laboratory animals and by Betts, Lamont and Littlewort (1960) for pigs, with the addition of the words " colostrum-deprived " to describe the immunological status of pigs obtained in this way. The difficulties are to detect the micro-organisms and then to decide which are natural pathogens. In practice all that can be done is rigidly to follow sterile routines in rearing the pigs and to examine thoroughly a small sample of the pigs.

Class III presents the greatest problem of all. The group is a very broad one, covering as it does animals kept under a wide variety of conditions of husbandry. Once adequate control procedures have been established it may be possible to limit the group or to sub-divide it. In the meantime the general term " minimal-disease " was coined by Betts, Lamont and Littlewort (1960).

The term widely used in the U.S.A. to describe both laboratory animals and pigs is " Specific Pathogen Free " (SPF). In the case of pigs at least it refers both to Class II and Class II animals but differentiates between foundation stock and the progeny by calling them " 1st generation SPF pigs," " 2nd generation SPF pigs " and so on. SPF pigs are regularly tested for the absence of certain specified diseases.

Since for practical purposes the disease status of the animal is all that matters, how the original microbiologically sterile stock was obtained from the uterus is of no great account, particularly since several methods can be used. Thus terms such as " hysterectomy-produced " and " Caesarean-derived " are of comparatively little value. The name " disease-free " embraces conditions of non-microbial origin and is therefore too inaccurate, while the description " clean " has obvious ambiguity.

Some of the difficulties of terminology may be removed when adequate control schemes have been established to maintain the status of the various types of gnotobiotes, but many of the problems of precise definition are likely to remain.

For the purposes of this paper Class II pigs will be referred to as " pathogen-free, colostrum-deprived " (PF) pigs, and Class III pigs, such as those in the herd at the School of Veterinary Medicine, as " minimal disease " (MD) pigs. When considering the American swine repopulation procedure the term Specific Pathogen-free (SPF) will be used.

Equipment and Operative Procedure for Hysterectomy

Details of the equipment, its construction and the operative procedure that we have found to be satisfactory have already been reported (Betts, Lamont & Littlewort, 1960). The operation is normally undertaken on sows at the 111th or 112th day of pregnancy. The sow is first stunned by means of electrolethaler tongs and then hoisted by her hind legs. A bag containing carbon dioxide gas, produced by pouring hot water over solid carbon dioxide, is placed over the sow's head and closed by means of a double draw string. At the same moment the electrolethaler tongs are removed. The sow inhales the carbon dioxide gas and becomes anaesthetised. During anaesthetisation the abdomen is scrubbed with 1 per cent. Cetrimide solution (B.P.) When anaesthesia is adequate the abdomen is opened. The whole uterus is removed and passed through an antiseptic lock into the body of a stainless-steel operating hood which has been previously steam-sterilised. After hysterectomy has been performed the sow is " bled out " and the abdominal wound closed with a continuous blanket suture penetrating deeply into the subcuticular tissues to ensure a water-tight closure and thus permit salvage for human consumption.

Once the uterus has been pulled up into the operating hood a trapdoor above the antiseptic lock is closed and the piglets rapidly torn out by two operators working through rubber gloves attached to the side of the hood. After clamping the umbilical cord of each piglet and breaking the cord distal to the clip, each piglet is wiped and dried vigorously using sterile hand towels. The umbilical cord is then ligated close to the abdomen, cut and dipped in tincture of iodine. The piglets are next put into a sterilised carrying case which is withdrawn from the side of the hood. As the case is withdrawn a sterile outer cover is slid over it. This outer cover is removed as soon as the carrying case is passed into the isolation pen containing the incubator units. With sterile precautions 1 pig is put into each stainless steel incubator unit. Each incubator is supplied with filtered air.

The piglets are fed 3 times a day on a commercially available sow-milk replacer (Amvilac No. 1, Glaxo). This diet is sterilised by autoclaving before being fed to the pigs in liquid form from flat stainless steel trays.

The piglets are removed from the incubators at about 14 days of age and are transferred to solid sided cages. In these cages, which are also kept in isolation rooms, they are weaned first to solid Amvilac No. 1 and then to pelleted food.

Results

Since we began this work in July, 1957, we have reared 72 litters. Of the 712 pigs obtained alive from the sows' uteri 595 have been reared giving an overall survival rate of 83.5 per cent.

Using the techniques actually described in this paper we have subjected 49 sows to hysterectomy. From these, 495 piglets were obtained alive and of these 435 were reared giving a survival rate of 87.9 per cent.

Some Uses of PF and MD Pigs

1. Research

a. *The Preparation of Tissue Cultures*

It is well known that, when tissues from ordinary animals are used for the preparation of tissue cultures, " wild " viruses are not infrequently isolated and these may cause degeneration of the cells. The presence of " wild " viruses in cultures of monkey kidney cells has often been reported. Hull, Minner and Smith (1956) and Hull, Minner and Mascoli (1958), discussed the problems that this may cause when working with human poliovirus. The problem is serious enough when cells from another host are being used, but when cells derived from the natural host of the virus under study are being utilised the problem is magnified. In our work we have frequently encountered cytopathogenic agents in cells derived from the kidneys of conventional (*i.e.* ordinary) horses and, to a lesser extent, from the kidneys of conventional dogs. Sometimes these cytopathogenic agents do not appear until the cells have been passaged serially several times or, after the control cultures have been kept for some weeks. When working with cultures derived from animals of unknown history there is always the fear that non-cytopathogenic viruses may be multiplying undetected in the cultures. Their presence might not be appreciated until the tissue culture fluids are inoculated into a susceptible host. It can readily be seen that " wild " viruses, whether cytopathogenic or non-cytopathogenic, can give rise to misleading or even utterly false results. For these reasons we have used PF pigs as far as possible for the preparation of porcine tissue cultures. When PF pigs have not been available MD pigs have been used. To date, after 4 years' work, we have not yet encountered any " wild " porcine viruses in cultures from such pigs.

b. *Studies on Pig Diseases*

The necessity of using experimental animals that are free from intercurrent infections and free from natural antibodies against the diseases under investigation has already been mentioned. This is particularly important when working with widespread diseases of low pathogenicity. Examples of such diseases are those associated with the porcine enteroviruses. Without the use of PF pigs many studies on these viruses would be impossible because of the high incidence of enteroviruses amongst conventional pigs.

PF pigs have been used in this country for studies on the pathogenicity and pathogenesis of a number of enteroviruses and for the production of type-specific antisera by Betts and Jennings (1960), Betts, Kelly, Lamont and Sheffy (1961) and Lamont and Betts (1960). Comparable studies have been made in the U.S.A. by Beran, Wenner, Werder and Underdahl (1960) and Singh, McConnell, Bohl and Birkeland (1960), and by Sibalin and Lannek (1960) in Sweden.

One of the original uses for PF pigs was for the

investigation of the virus of transmissible gastroenteritis (Young & Underdahl, 1953; Young, Hinz & Underdahl, 1955). Later, Goodwin and Jennings (1959) used some for studies on a transmissible gastroenteritis of pigs in this country. Other work in which such pigs have been used by various workers in this country and abroad include studies on virus pneumonia of pigs, swine influenza, a pleuropneumonia-like organism recovered from the upper respiratory tract of pigs, some other respiratory infections and some enteric infections.

c. *Other Types of Research on Pigs*

For any type of biological research it is necessary to reduce extraneous variables to a minimum. Of the variables that beset work involving animals disease is perhaps the most difficult to control. Thus pigs which are free from infectious diseases have obvious advantages for investigations on nutrition, housing and genetics. The techniques and equipment used for producing PF pigs also permit critical evaluations to be made of the nutritional requirements of the young pig.

d. *Some Diseases of Man*

It has been known for a considerable time that very young animals may be susceptible to virus diseases which do not affect adults of that species. For example, suckling mice can be infected with Coxsackie viruses of man and with the virus of foot-and-mouth disease whereas adult mice are refractory. Again, embryonated hens' eggs are susceptible to a number of viruses which do not affect adult chickens. The very young PF pig has the additional advantage of being devoid of gamma globulin and thus there is some justification for thinking that it might be useful in the study of certain diseases of other species including man. A group of viruses affecting man for which there are, as yet, no recognised experimental animals is the adenovirus group. However, Guerin and Guerin (1957) showed that some adenoviruses could be grown in porcine kidney monolayer cultures. Following this lead Betts, Jennings, Lamont and Page (1961) grew various adenoviruses in porcine kidney cells and then investigated the pathogenicity for PF pigs of some of these, particularly adenovirus type 1. Lesions were produced in the respiratory tract of PF pigs inoculated between 1 and 2 weeks of age by the intranasal or the intratracheal routes. Macroscopically, there were areas of consolidation, sometimes extensive, and the bronchial lymph nodes were markedly enlarged. Histologically the lesions were those of collapse, bronchiolitis and alveolitis; many of the bronchial epithelial cells and the alveolar cells contained activated nuclei and adenovirus-type inclusion bodies were present. Lesions appeared to reach their maximum about 8 days following inoculation. In the early stages of infection virus could be recovered from the lung, trachea, bronchial lymph nodes and tonsils but at later stages it could be recovered only from the lungs. Infection could be transmitted from pig to pig by intratracheal inoculation at least for a limited number of passages. Further work with this adenovirus and others is in progress.

2. The Control of Pig Diseases on Commercial Farms

At the time of writing at least 4 commercial companies have been formed in this country to produce pigs by hysterectomy (or other means) for the repopulation of farms, but repopulation is still very new and still on a small scale. However, one herd that was established entirely from PF pigs and which has been in existence for some years is the " minimal disease " herd at the School of Veterinary Medicine, Cambridge. This was derived from the progeny of 5 pedigree Landrace sows which were subjected to hysterectomy. Nine gilts and a number of young boars were selected from the progeny of these pigs and in September, 1958, were transferred to the farm of the School of Veterinary Medicine. They were housed in fold-units which had been cleaned and disinfected and were on pasture. During the first few weeks under farm conditions there was a little diarrhoea and some pigs did show a mild febrile condition but there were no losses. Since then the health of the herd has been good; the herd now contains 22 sows.

In the U.S.A., on the other hand, repopulation of commercial farms with pigs taken usually by hysterectomy began in 1957 and the procedure has now become widespread. The programme was reviewed recently by Betts and Luke (1961).

a. The Specific Pathogen-free Pig Programme in the U.S.A.

In order to keep the American SPF pig programme in perspective, it is essential to bear in mind that the standard methods of pig husbandry in the U.S.A. differ markedly from those customarily seen in this country. Farrowing is virtually confined to the spring and autumn and almost all pigs are finished in " hog-lots," which are comparatively small areas of land that have often carried pigs for several decades. Maize provides the principal feeding-stuff and the main source of protein is soya bean. The vast majority of fattening pigs are fed *ad lib.* from self-feeders. The main emphasis is laid on growth-rate and few, if any, records of food conversion rates are kept.

The Repopulation Procedure

The expensively-equipped commercial centres at which the primary stock for repopulation are produced are all licensed and all are operated by veterinarians. When a farmer wishes to repopulate his farm with the progeny of his own stock, he sends to the centre a group of sows which are expected to farrow at approximately the same time. At the centre hysterectomy (usually) is performed on the 110th to 112th day of pregnancy using techniques closely similar to those described earlier in this paper. The main differences are that the piglets are usually fed a diet composed of cow's milk, eggs and minerals and that they are removed from the incubators at 7 to 10 days. After this they are placed in brooders

(Underdahl & Young, 1957). In general the piglets are kept in the brooders until they reach 4 weeks of age, at which time they are returned to the farm.

After sending sows to the veterinary centre the farmer removes all pigs from his premises, which are subsequently cleaned thoroughly and left empty for 4 to 6 weeks. After the 4-week-old pigs have been returned to the farm they are usually subjected to a short period of conditioning. Thereafter normal rearing procedures are followed except that no pigs other than SPF stock are introduced to the farm and contact with conventional pigs is avoided. When the primary SPF pigs reach maturity they are used as the foundation breeding stock. Then the herd is treated as a normal breeding herd, except for the rigid precautions which are necessary to prevent the introduction of infection from outside. From the primary herds established in this way secondary herds can be formed on other farms which have, in turn, been depopulated, cleaned thoroughly and rested for 4 to 6 weeks.

The extent of the Swine Repopulation Programme

The programme has undergone rapid expension in the U.S.A. during the past year or so and appears still to be extending. Training courses have been organised by the University of Nebraska to provide specialised knowledge on the techniques for producing and rearing SPF pigs and nearly 150 veterinarians from the U.S.A. and Canada have attended them. A conference of veterinarians on advances in swine repopulation was also held in June of this year. By the spring of 1961, 69 licences (see later) for the production of primary stock by hysterectomy techniques had been issued, although not all these licensed veterinarians were in action at the time of writing. The output from those centres which were in production then was estimated to be about 7,000 pigs per month.

The first SPF herds were established on commercial farms in 1957. Young (1960) reported that by the end of 1960 more than 1,000 primary herds would have been established.

The Performance of SPF Pigs

When visiting certified SPF herds the absence of "runts" and the "even" appearance of the pigs is noticeable. Owners are extremely enthusiastic but there is comparatively little factual information available on performance of the pigs. Almost all the information that is available comes from Nebraska. The performance of herds in the SPF programme supervised by the University of Nebraska is given in Table I (Welch, 1961). For the purposes of rough comparison the 1958 herd analysis of the Wisconsin Swine Selection Co-operative is included since this does give results obtained by some of the better swine producers in the U.S.A. with conventional pigs kept under approximately similar conditions.

The difficulty in obtaining food conversion figures for SPF pigs has already been mentioned. The only figures that seem to be available come from the University of Nebraska's experimental herd. Peo and Hudman (1960) compared the performance of SPF pigs with genetically similar conventional pigs (designated "contaminated") kept under identical conditions with the results shown in Table II.

From personal observations and discussions with many veterinarians concerned with the programme, it appears that the swine repopulation procedure in the United States has proved to be an effective method of eradicating respiratory infections, such as virus pneumonia, and external parasites, such as mange. Intestinal problems seems to be less but, not unexpectedly, there has been no noticeable effect on infections with ascarids or lungworms. When the SPF programme began fears were expressed that young SPF pigs would be very susceptible to a variety of infections when returned to farms and would probably die. These fears have not been borne out in practice. However, there is a "lag period" of a few days before the pigs begin to thrive. The overall mortality rate amongst 1st generation SPF pigs seems to be of the order of 2 to 3 per cent. Caldwell, Sumption and Young (1959) have produced evidence to suggest that adult SPF pigs at least are as resistant as conventional pigs

TABLE I

SUMMARY OF THE PERFORMANCE OF SPF PIGS ON NEBRASKA FARMS (FROM WELCH, 1961)

	Number of herds	Number of litters	Average size of litter		Mortality rate to 56 days (per cent.)	Average pig weight at 56 days in lb.	Average pig weight at 154 days in lb.	Average daily gain 56–154 days lb. per day
			Born	Raised to 56 days				
1958 Spring	6	33	11·2	9·2	17·1	47	213	1·69
Autumn	6	36	10·2	8·2	24·9	37	179	1·45
1959 Spring	11	105	9·8	8·4	14·1	43	201	1·61
Autumn	11	108	10·2	8·4	17·2	45	213	1·71
1960 Spring								
All SPF herds	14	156	9·7	8·0	17·7	44	199	1·58
Certified SPF herds	10	126	10·1	8·3	17·4	45	206	1·64
Wisconsin Swine Selection Co-operative Herd Analysis (1958)	70	430	9·5	7·6	22·1	N.G.	155	NG

NG = Not given.

TABLE II

COMPARISON OF PERFORMANCE OF CONTAMINATED AND SPF GROWING-FINISHING PIGS*
(PEO & HUDMAN, 1960)

	Number of pigs	Initial weight in lb.	Final weight in lb.	Average daily gain lb. per day	Food conversion rate	Season
Contaminated ...	68	22·4	168·0	1·43	3·44	Autumn 1957
SPF	84	22·6	177·5	1·58	2·98	Spring 1958

* These pigs were Large White/Hampshire crosses.

and they placed SPF boars in "ordinary" (*i.e.* infected) pig herds without dire consequences.

Problems encountered

Inevitably problems have occurred as swine repopulation has become extensive, although some of the difficulties appear to be of the participants' own making. On repopulated farms the most important single problem appears to be infection with helminths, and some severe infestations with ascarids have been encountered. Under the "hog-lot" system of keeping pigs it is difficult to see how heavy infections can be avoided. In general, ascarid infection amongst pigs is a much greater problem in the U.S.A. than in this country.

Nutritional problems have occurred with some SPF pigs and this may be associated with the increased growth-rate. There is some evidence that higher levels of vitamin and mineral supplementation may be needed for these pigs.

The main problems for those operating the primary production centres are the heavy capital expenditure required to establish the centres, the high degree of professional skill and training needed to produce consistently healthy pigs of the proper standard and to place them successfully on farms, the importance of obtaining accurate service dates and the careful selection of the client.

Control Measures

The necessity for adequate control procedures to ensure the quality of primary stock coming from primary production centres and the maintenance of the status of SPF stock on farms subsequently was appreciated at an early stage.

The production of primary SPF stock in the U.S.A. is, therefore, now restricted entirely to registered and approved veterinarians by means of licences issued by the University of Minnesota. The University holds 2 patents covering the technique for obtaining the piglets from the uterus, the design of the hood used to remove the pigs from the uterus and the brooder equipment. Normally each licence is automatically renewed annually, but it can be cancelled for a number of causes. These include misrepresentation of facts essential to the establishing of the licence and failure to maintain the standards set up by the National Swine Repopulation Association. The number of licences issued is restricted and normally only 1 licence is issued per 1 million pigs in the area. This restriction is based largely on economic grounds since it has been calculated that a pig population of this size is necessary to support each properly equipped and staffed primary production centre. The strict licensing system and the specialised training provided by the University of Nebraska have undoubtedly helped to reduce the number of problems which might have occurred in connexion with the operation of the primary production centres.

The National Swine Repopulation Association referred to above was formed to conduct professional activities in connexion with swine repopulation. It also promotes programmes of certification and accreditation of repopulated pig herds and the primary production centres.

The current Specific Pathogen-free certification programme sponsored by the University of Nebraska is both an ambitious and an optimistic one. Not only does it cover a number of diseases but it also includes basic performance figures which must be achieved before a herd can be certified. The inclusion of the performance figures is to ensure that only good quality stock are used as foundation stock for repopulation purposes and in the hope that performance figures might act as a rough measure of the presence or absence of diseases, as yet undefined, but which might affect production. The health requirements for certification are vaccination against swine fever, freedom from brucellosis and swine dysentery, freedom from virus pneumonia and atrophic rhinitis, freedom from external parasites and freedom from leptospirosis. The tests for virus pneumonia and atrophic rhinitis are based on examination at slaughter of the lungs and snouts on a statistically determined sample of pigs from the farm. The diagnosis of leptospirosis in a herd does not necessarily disqualify that herd from certification completely, but stock must not be sold until 30 days after the disease has been brought under control by treatment or vaccination. In the case of certain other infectious diseases SPF stock must not be sold until 30 days after the disease has been brought under control by vaccination or treatment or has become quiescent. Certification is not withheld because of infection with internal parasites. Nor is it withheld in the case of certain other enteric infections such as transmissible gastroenteritis (TGE) but the certificate must state clearly that TGE has occurred in the herd from which the stock originated. To achieve certification the herd must conform to the performance standards. The minimum

average performance figures are 155 lb. weight at 140 days of age and a maximum backfat thickness of 1.5 inches as shown by probing. Boars must achieve appreciably higher standards before individual certification is given, and no individual certification is given unless the herd average reaches the prescribed standards.

Comment

Many questions are yet unanswered but there seems little doubt that, at the present time, the production of SPF pigs in the U.S.A. is both worthwhile and successful. The most apparent effects of swine repopulation are in the control of respiratory infections and external parasites. Most people consider that the elimination of these conditions alone justifies the production of SPF pigs. Under the American system of pig husbandry it seems unlikely that much more than this can be achieved from the overall programme when sales made from secondary herds increase in number.

The control of the primary production centres is good but control of the secondary producers poses a much more difficult problem and is therefore less effective. The major difficulty the ambitious SPF certification scheme is likely to encounter will be that of specific diagnosis resulting mainly from the general lack of knowledge concerning diseases affecting the pig. But even in the light of existing knowledge the criteria on which freedom from VPP and atrophic rhinitis are judged seem to be open to serious criticism. Apart from the problem of diagnosis the certification scheme is likely to be expensive to operate and, since it is voluntary, some of its standards may be difficult to enforce. An encouraging feature of the whole scheme, however, is that both the production of SPF pigs and the certification programme are solidly in the hands of veterinarians who have had specialised training in the subject.

b. **Swine Repopulation in the United Kingdom**

If swine repopulation succeeds under the somewhat haphazard conditions of pig husbandry in the U.S.A. it could be equally successful, or even more successful, under the conditions of pig husbandry that exist on progressive pig farms in this country. But whether swine repopulation will succeed or fail will depend largely upon the steps that are taken now to ensure that the stock coming from the existing and proposed primary production centres are indeed free from infectious diseases, and the measures adopted to maintain the status of pigs on repopulated farms. As in the U.S.A., control procedures therefore fall into 2 parts.

1. *Control of Primary Production Centres*

The primary production centres can only produce pigs that are consistently free from infectious diseases if they are properly equipped with incubators, brooders and sterilisers, and the personnel are fully trained in all the necessary procedures.

At present the prospective purchaser has virtually no protection against deception since there is no independent control over the centres, and the hysterectomy procedure when performed at slaughter may be outside the Veterinary Surgeons' Acts. There seems to be little to stop untrained lay people attempting to produce pigs under the most unsatisfactory conditions and selling them, at least by implication, as pigs produced by hysterectomy and therefore free from disease.

To deal with this situation there seems to be a strong case for legislation along the lines of that governing the operation of Artificial Insemination Centres. Under such suggested legislation each primary production centre would be licensed by the Minister of Agriculture and be subject to certain conditions. These would be designed to ensure that each primary production centre was under the effective supervision and control of an approved veterinary surgeon, that the lay technicians were adequately trained, that the premises, equipment and techniques used were satisfactory and that sufficiently detailed records of such items as the numbers of piglets reared and addresses of repopulated farms were kept.

Regular inspection of the primary production centres would not be particularly difficult since, on economic grounds, the pig population of the country is likely to be able to support only 4 or 5 adequately equipped and staffed centres.

2. *Control of Repopulated Herds*

A control scheme for pigs on repopulated farms will undoubtedly be difficult to operate, controversial and expensive. It is nevertheless essential if swine repopulation is to succeed. There are many aspects of the problem which need to be considered by representatives from all the bodies concerned as a matter of urgency.

Some points which need consideration are:—

a. Whether the control scheme should be a voluntary one run by an impartial farmers' organisation or by a veterinary organisation, or whether it should be an official one. For any extensive control scheme a full-time veterinary staff will almost certainly be necessary and laboratory facilities required. Because of the expense this would entail, support from official sources would probably be needed even by a voluntary scheme. A widespread control scheme operated by a lay organisation might raise questions of principle and ethics.
b. The diseases to be covered by the control scheme.
c. Whether basic performance figures should be included and, if so, how this could be integrated with pig recording schemes such as those operated by the Pig Industry Development Authority.
d. The procedure to be adopted in the event of a "breakdown."

Swine repopulation appears to have considerable potential value for the pig industry of this country and if it succeeds in reducing the disease burden of the national pig herd, it could lead to radically different and more intensive methods of pig husbandry. In its wake it will bring new problems,

responsibilities and opportunities for veterinary surgeons as it is already doing in the U.S.A. Only a small number of veterinary surgeons are likely to be concerned with the primary production centres but the repopulated farms will be the concern of many.

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The Speaker's Introduction

The Chairman, Mr. J. A. de Garis, welcomed Dr. A. O. Betts, who had been working both in this country and America. Obviously those present did not want to hear from the Chairman so he would call on Dr. Betts straight away to open his paper.

Dr. A. O. Betts said that it was always an honour to be asked to talk to a scientific meeting, and most of all at one of the British Veterinary Association. He felt a sense of humility in speaking on this occasion for two reasons. At the meeting was Mr. Underdahl who, with Dr. Young, had done so much pioneer work in the United States on the subject of specific pathogen-free pigs. It was 5½ years ago that he had first met Mr. Underdahl and Dr. Young and had spent several weeks in their laboratory, being initiated into some of the mysteries of producing SPF pigs. It was from that initiation that the techniques used at Cambridge had been evolved. The second reason was that the subject was extremely new. It was a highly complex one, and although work at Cambridge had been going on for over 4 years, neither he nor his colleagues would claim to know very much about the subject. They were conscious of their lack of knowledge of many aspects.

The printed paper dealt with the use of "pathogen-free" pigs for research and for the establishment of minimal disease herds in the field. Since time was short it was on the latter subject, which was both difficult and controversial that he intended to spend most of his time.

Those who were keeping up with current news would appreciate that those competent to judge agreed that the changes of emphasis in official policy which had been forecast, coupled with the implications of joining the European Common Market, meant that higher production plus better quality at lower cost was likely to be the only key to success for British agriculture in the future. In no branch of agriculture was that likely to apply more than to pig production.

These developments, mostly during the last year, if they had done nothing else, had underlined the remarks made by Professor Beveridge in his Congress paper last year on the vast economic losses which were caused by apparent disease, and perhaps more important, inapparent disease. It seemed reasonable comment to suggest that the pig industry in future probably would not be able to afford that level of loss. Therefore a method of disease control which aimed to deal with a number of diseases at one blow became of somewhat more than mere academic interest.

In the U.S.A. repopulation with "minimal disease" or "specific pathogen-free" pigs was now extensive. By the spring of this year, 69 licences had been issued to approved veterinarians to operate primary production centres producing SPF pigs, and from those actually in production, about 45 in number, the potential output was estimated to be 84,000 pigs a year. It had also been reported by Dr. Young that, by the end of 1960, over 1,000 primary herds would have been established.

Already in this country a small number of companies appeared to be planning to produce such pigs and, judging from advertisements and articles in the agricultural press, one had already begun to sell pigs. But since repopulation was in its infancy in this country, most of his remarks on swine repopulation must of necessity be based on American experience.

To produce "pathogen-free" pigs successfully, whether for research or for subsequent repopulation, there were two essential steps. The first was the removal of the unborn piglets from the uterus of the sow in a microbiologically sterile way up to 3 days before normal parturition. That could be done by hysterotomy, provided an elaborate and sterile technique was used, but until an appreciably simpler hysterotomy technique had been perfected, hysterectomy was more likely to be used.

The second stage was the rearing of the piglets for 7 to 14 days in sterilised incubators in isolation rooms on a sterilised diet.

A number of slides were then shown illustrating the methods used at Cambridge.

For the first few days in the incubators, the piglets were very susceptible to infection, possibly even to some human infections.

If the pigs were ultimately to be used for farm repopulation purposes, they next needed to be "conditioned." The usual procedure was to rear them in groups in brooders until they reached 4 to 5 weeks of age. Under the American system they were then returned to the farm which had previously been emptied of pigs, cleaned, disinfected and rested for 4 to 6 weeks.

After the pigs had been returned to the farm, stringent precautions had to be taken to prevent the entry of infection. Otherwise the pigs were treated as ordinary pigs.

The reduction in the disease burden which had occurred following the repopulation of herds in the United States appeared to have improved productivity considerably, although factual information on that point was not as extensive as one would like. In assessing the American results one also had to bear in mind that methods of pig keeping in the U.S.A. differed markedly from those practised in this country.

There were obviously 3 essential elements if a swine repopulation programme were to be successful on a large scale. Firstly, the stock coming from the primary production centres must be free from infectious disease. To achieve that it was necessary that the personnel at the centres be highly trained and that they had adequate facilities. That in turn necessitated the expenditure of a great deal of capital on buildings and equipment. The procedure followed must also be beyond question. To ensure that those requirements were always met, it was virtually inevitable that there must be some independent control over the primary production centres.

Secondly, steps had to be taken to maintain the health status of pigs on the repopulated farms. Once again, it was difficult to see how that could be achieved without some measure of control by a totally impartial organisation.

The third essential was education. It was necessary to have means of conveying information to veterinary surgeons on the technique of repopulation and the problems which were likely to be encountered. In addition, farmers needed to be educated on the different management methods which would be necessary to keep out disease and to obtain the maximum productivity from the pigs.

Those 3 elements had been recognised in the U.S.A. All the primary centres were licensed, and licences were only issued to approved veterinarians. There were also voluntary schemes for the control of repopulated herds. They covered various diseases and it was also required that the performance of the pigs on the farms reached certain basic standards.

As far as education was concerned, getting information over to the public and to veterinarians was a field in which the Americans excelled. For veterinarians there had been a number of training courses provided by the University of Nebraska.

In this country, one immediately came up against serious problems. At the moment, there seemed no way of controlling the primary production centres, as far as he could determine. The hysterectomy procedure when it was performed at slaughter was probably outside the Veterinary Surgeons Act. Thus there appeared to be little or nothing to stop untrained lay personnel attempting to produce those pigs under very unsatisfactory conditions. For example pigs could be taken by hysterectomy in a slaughterhouse without using an operating hood and reared in contact with conventional pigs on foster mothers or with the help of serum and antibiotics. Such pigs could, quite truthfully, be sold as "hysterectomy-produced" irrespective of their disease status. Unfortunately to many people the term "hysterectomy-produced" was synomymous with "disease-free."

Thus the production of pigs for repopulation purposes was open to abuse. What could be done about it? His opinion was that one of the most effective ways of dealing with the problem would be to have some kind of legislation along the lines of that governing Artificial Insemination Centres. Under such legislation each primary centre would be under the effective control of a veterinary surgeon. Lay technicians would have to be adequately trained; the Ministry of Agriculture would see that the premises, equipment and techniques used were satisfactory, and that the proper records were kept in case anything went wrong.

On the basis of American figures it was unlikely on economic grounds that the pig population of this country, running as it did at 5,000,000 or so would be able to support more than 4 or 5 adequately equipped and staffed centres, so it was obvious that the inspection of primary centres would not be an insuperable problem. He realised there were great difficulties in initiating legislation but felt it was worth serious consideration.

As far as control of repopulated herds was concerned, it was obviously going to be extremely difficult to devise a workable scheme, but he felt that one was essential. It would be expensive to operate and there were a number of opposing interests to be considered. The situation could perhaps best be tackled by having, as a matter of urgency, a meeting of representatives of all the bodies likely to be concerned in order to see whether they could produce an effective scheme.

Until veterinary control of swine repopulation had been established there was an educational problem additional to that already mentioned. It would be necessary to convince the farming community of the need for close veterinary supervision of all aspects of swine repopulation. Such supervision was obviously in the interests of agriculture. It was not without its importance for the profession.

Finally, repopulation in the U.S.A. at the moment was confined to pigs but already experimental work had been done with sheep and other species. It might be worth contemplating the possibility that similar repopulation procedures might one day be used for other species of animals.

A film was shown which reviewed the method of producing "pathogen-free" pigs and their uses.

The Opener

Mr. M. R. McCrea said that all present would agree when he said that Dr. Betts was to be congratulated for discussing such an interesting topic so ably in his paper, and by illustrating it so well in the excellent film they had seen. Endeavours such as those necessitated team-work, and it was obvious from the results presented that the Cambridge School had a very efficient and active team as far as the production of pigs by hysterectomy was concerned. Some may have seen a previous film about the actual technique of removal of the litter from the sow. He thought he was right in saying that it was made with some time-and-motion studies in mind for all the operators and assistants wore large numbers on their backs. The activity in the film was tremendous; a knife being wielded here, a needle there, and numerous assistants scurrying to and fro all intent on their predetermined functions. His impression after seeing it was of an ants' nest disturbed and tormented by a mischievous boy, only in the film the ants did not carry pupae in their jaws but large numbers on their backs.

He mentioned the earlier film for two reasons. One was to underline the fact that considerable organisation and capable administration was necessary; the second was to remind those present that a lot of elaborate equipment was required for the work, and in that respect, the American concept of a "centre" seemed sound, based on one per million pig population and, as Dr. Betts said, about 5 would be required for England and Wales. However, in his paper, he mentioned that hysterectomy was not the only method of obtaining microbiologically sterile pigs from the uterus, and that, at Cambridge, they were experimenting with other methods. Would he say more about that?

Though expensive equipment and heavy labour requirements were concerned with the rearing of the pigs, particularly in the early stages, it was interesting to note that under conditions of general veterinary practice in this country, the work was being tackled. Rearing arrangements were simplified in that case for the piglets were required as potential breeding stock to be introduced into a virus pneumonia-free herd and they were fostered on to suitable sows in that herd. There was a good example by Mr. Morgan and his colleagues at Chepstow of the application of the whole concept of breaking the cycle of disease between dam and offspring.

The idea of producing, rearing and using germ-free animals for experimental work had been pursued by Professor J. A. Reyniers and his colleagues of Notre Dame University, Indiana, for over 30 years. Two years ago, at the Folkestone Congress, Dr. E. L. Taylor in his paper on "The Relationship Between Intensive Agriculture and Animal Disease" drew attention to what he called "some strange procedures" that those workers had to undertake "in order to separate experimental animals from their microbial associates." With their supersterility techniques, the workers at Notre Dame were able to maintain animals free of micro-organisms indefinitely, but there had been some unusual side results on which he would be interested to have Dr. Bett's opinion. Firstly, had he noticed any peculiarities of behaviour in the isolated piglets? In the earlier work with rats at Notre Dame deaths were occurring because the baby rats were not urinating at all; they apparently did not know how to. It was found that stroking the genitalia initiated urination and thereafter no stimulus was needed. In nature no doubt licking by the mother got over that little difficulty. The relative proportions of the tissues of the germ-free animals were different, too, when compared with the conventionally-reared. Their lungs and intestines had less lymphoid tissue and their livers were smaller. As both the lymphoid tissue and the reticuloendothelial tissue (and the plasma cells) were sites of antibody production and the animals had no antibodies, nor any need for any, one might consider that those differences occurred for that reason. Had Dr. Betts any information on those lines from his pigs? Did they differ structurally from the conventionally-reared pig?

Instead of "conventionally-reared" pig, he might easily

have said "normal" pig. Which was to be the "normal" pig? That led for a moment to the question of terminology which Dr. Betts had tackled in his paper. It was very necessary to have the terms most carefully defined, because, as had been pointed out, the whole technique could easily fall into disrespect if the various groups were not exactly what they were called. The terms "germ-free," "pathogen-free colostrum deprived" and "minimal disease" seemed reasonable for the 3 classes Dr. Betts had described. Dr. Betts could not be blamed for the term "gnotobiotes"; he made clear that it was not his responsibility.

Dr. Betts mentioned that germ-free animals were free from gamma-globulin for a time. Why should they not remain free indefinitely, or did the appearance of antibody indicate some breakdown in the technique? However, it would appear that germ-free pigs would prove extremely useful experimental animals for the study of pig diseases, and particularly the clarification of some of the mysteries of immunity.

The diet used for rearing the pigs at Cambridge was a proprietary one. He presumed a special form of that diet was used, as it normally contained penicillin. One of the points made by the Notre Dame workers was that antibiotic supplementation of the diet of germ-free animals did not increase growth rate. At the same time, it was interesting to note one report where pigs obtained by hysterectomy and maintained in isolation units responded, in that case, to a diet supplemented with chlortetracycline. In an earlier paper about the position in America, the author mentioned troubles of a nutritional nature as being a problem, the increased growth rate causing greater demands for vitamins and minerals. Had Dr. Betts met that with his own pigs?

The author had considered the uses of the germ-free pigs under two main headings: for research and in the field. As far as research was concerned, they obviously had many and important uses. As long ago as 1953, Young and Underdahl reported their use for investigations on transmissible gastro-enteritis. He believed Dr. Underdahl was in the audience and they looked forward to hearing from him in the discussion. Further refinements of the technique might well make germ-free pigs less expensive experimental material, while in the interim period, there was still a place for the early-weaned pig as an experimental animal for many purposes. Looking ahead, it was possible to envisage, for nutritional studies at least, that work done with germ-free pigs might have to be repeated in the more conventional types of experimental pig before the results could be applied to farm conditions. Otherwise, great expectations might not be fulfilled.

In the field, the technique was a powerful tool in Preventive Veterinary Medicine. The clean cut that could be made between infected dam and offspring with diseases such as virus pneumonia and mange was a striking example. However, it was so easy for a matter like that to get out of hand; too much was expected as a result of insufficient testing of the preliminary work. It had happened with early weaning of pigs on a commercial scale, and now the veterinary profession should ensure that repopulation procedures were a success. As Dr. Betts pointed out, now was the time to act and the organising committee for the Congress was to be congratulated for selecting so topical a subject for discussion.

Leaving aside questions of disease and considering those of husbandry, with which he was more familiar, a problem arose. The technique as it stood at the moment entailed the sacrifice of the sow. For progress to be made, repopulation should be done with the offspring of the best progeny tested sows but the genetic potential of those sows was going to be sharply curtailed by their slaughter. The dangerous alternative was that farmers were going to accept pigs for repopulation of their herds just because they came from a repopulation centre, and their subsequent performance may well not match that of their genetically superior but subclinical disease-ridden fellows. The specific pathogen-free certification scheme run by the University of Nebraska that Dr. Betts mentioned was useful because it covered performance at a high level.

When discussing repopulation in this country, the author was disturbed because of the possibility of the hysterectomy procedure being outside the Veterinary Surgeons' Act of 1948. That was obviously a question that needed clarifying urgently, but he wondered what the specific point was that Dr. Betts was concerned about. In the 1st Schedule to the Act "The destruction of any animal by painless methods" could be done by a non-qualified person, but he did not see how the procedure of hysterectomy could be covered by that phrase. It was also possible for the Minister of Agriculture to specify by order, after consultation with the Council of the Royal College of Veterinary Surgeons, any minor operation which could be carried out by unqualified persons.

Finally, was there not still time to clarify the relationship between disease, "subclinical disease," and production?

He envisaged a piggery of minimal disease pigs, one of pigs with virus pneumonia, one of pigs from a VVP-free herd, and one of pigs being tested against each other in every conceivable way. There were Research Centres in this country where it could be done, and it should.

The General Discussion

Dr. R. F. W. Goodwin (Department of Veterinary Clinical Studies, Cambridge) said that he had been using colostrum-deprived piglets since 1958, when Dr. Betts had first made them available for research but, more recently in a respiratory-disease research programme, they had found the second-generation pigs particularly useful for two reasons: first of all they were cheaper and, secondly, they were much more robust. They had occasionally run into trouble when using the first-generation pigs because these had died before the results of infective transmissions had been obtained. His main interest, however, was in the field side, rather than the laboratory approach, and he wished to enlarge upon a few aspects of that. It rather followed on something that Mr. McCrea had said about the need for more information on the performance of hysterectomy-produced pigs on farms.

He was associated with a company that had been producing such pigs commercially since February this year, and hence the litters had been going out onto farms under ordinary commercial conditions for some time. The problem that Mr. McCrea had posed was very important; more information was needed about the performance of these pigs under British conditions, and information from America should not be transferred unquestioningly.

He had managed to persuade the company that they should provide him with a number of litters—in fact nearly the whole output—to test out certain facts. Two main things were being done: the litters were being put out onto farms at different ages, to see how viable they were at different stages of development and how young they could be safely exposed to risk, and, secondly, he had been dividing the litters into half and distributing the 2 groups from each litter to herds where the disease-status had been followed for some time—enzootic-pneumonia-free herds and herds free from a variety of respiratory diseases. One half of the litter had been brought into the herd and the other half kept in isolation; the 2 halves of each litter were being recorded throughout, as regards both health and performance. He hoped that food-conversion figures would also be available eventually for intra-litter comparisons. It was too early yet to summarise the findings, but he hoped fairly soon to have some figures, urgently needed in this country, about the performance of hysterectomy-produced pigs on different farms, under different husbandry conditions, on different rations, with different levels of competence at the managerial and pigman levels. In each case, the performance of the pigs would be contrasted with both the average performance of more conventional pigs on the same farm and, as far as the pigs reared in isolation were concerned, their litter-mates.

The only thing comparable to the Young and Underdahl SPF control movement in this country was the enzootic-pneumonia control movement, which was confined to one disease. That movement was now screening 75 herds in Britain, of which over 50 had passed the veterinary standards; which means that about 50,000 to 60,000 fattening pigs a year were being checked for a variety of respiratory diseases. When one got involved in practical problems of that type in the field, one had to recognise certain facts. It was becoming clear that even among the most progressive

farmers in this country—such as those who had been the first to establish pig herds free from enzootic pneumonia—there were a number who were not sufficiently careful or fortunate to maintain even the enzootic-pneumonia-free status of their herd. There had been breakdowns for apparently simple reasons. Attempts to maintain herds free from a whole variety of diseases, and particularly diseases that could spread by indirect contact, would inevitably run into the same problems, but on a far bigger scale—the problems of the competence of ordinary farmers.

He was also currently engaged in advising what were coming to be called in the pig industry "pig empires"; one of the largest of these, for example, was planning to market perhaps about 1,000 pigs a week. That was something quite outside the ordinary concept of pig production in this country up to now, and it was bringing him up against considerable disease-control problems. In that situation, therefore, one had to face up to the very big question of where one set one's sights, and what was to be aimed for in the level of disease control. That then brought them right into the question of the licensing of stations.

Primarily, both in America and in this country, the whole hysterectomy technique had been developed for laboratory research, and the laboratory atmosphere had been too readily transferred to the field. What might be absolutely essential for laboratory research might turn out to be superfluous on a farm. Much thought in the pig industry was now being given to what diseases could be eradicated, and what diseases would be permanently worth eradicating from a pig population. They did not know; that was why preliminary experiments were being done. How much would be gained by eradicating diseases beyond the infectious, endemic respiratory diseases? If it proved that little would be gained, there would be a place for a variety of techniques much less elaborate than those used at the Cambridge Veterinary School. Already, farmers within the enzootic-pneumonia control scheme had had hysterectomies done on their farms by practitioners, the litters being transferred to foster mothers (free of the major respiratory diseases) for rearing. Pigs could be produced free of respiratory diseases merely by removing them from the sow at birth. The technique ultimately employed in different stations or in different circumstances, therefore, would depend entirely on the end result required. Very much more attention should be given to the end results, and less to one particular technique which was, in itself, an operation that could soon become a routine.

Why should a farmer have to eradicate more diseases than he thought justified? Dr. Betts had called for primary production centres to be licensed by the Ministry of Agriculture, but what would these centres be licensed to do? He saw no reason why a variety of different standards should not exist, depending on what service the customer wanted. Very serious questions were raised in Dr. Betts' suggestion, concerning the freedom the farmer had to do what he judged to be sound, and the freedom that a veterinary surgeon had to provide what the farmer wanted. A compulsory licensing system to the laboratory standards that Dr. Betts desired might compel the use of sledge-hammers of the type necessary for research on entero-viruses, etc., to crack some not particularly hard disease-control nuts (as far as disease eradication in the field was concerned).

It had to be remembered that, in America, they had gone in one jump from herds seriously affected with enzootic pneumonia and atrophic rhinitis (the main reason for the SPF programme) to so-called "pathogen-free" pigs. In this country, there was a less ambitious control scheme for enzootic pneumonia, and the possibilities of controlling other respiratory diseases were being explored. That was a very important difference. There was a half-way house already available, and there was the opportunity, therefore, to compare the relative economic advantages of different approaches.

Dr. R. Braude (Shinfield) thought that here was a potential tool which might lead to great things in the future, but, at the moment, too little was known about it. There were several points on which he had misgivings and he hoped that those would be proved to be incorrect, and that in the future the industry would benefit from the new development.

One major misgiving was that it was not at the moment known how long the herds, which had been established with so much effort could be maintained free of disease. If freedom from a specific disease was only temporary then too much effort was put into achieving it; if, after a year or two, the position was found to be similar to that at the start then a lot of time would be wasted on something which was not really worth while.

The other misgiving was that there was no scientifically sound evidence to show that the performance of the minimum disease pigs was better than that of pigs from really good herds found all over the country. The figures quoted by Dr. Betts were very interesting but they were from one small experiment, and that was not sufficient evidence. He had seen figures showing the opposite picture.

Taking the American conditions, as Dr. Goodwin pointed out, one of the major features was that they had been riddled with rhinitis; that was not so in this country—the problem of atrophic rhinitis did not exist here. One should be very careful in comparing the situation in the two countries.

In this country, herds were being freed from virus pneumonia quite successfully by other means. There was quite a lot of controversy, to which he did not subscribe, that the improvement in performance was not as striking as some people wanted to believe. In the herd with which he was connected, which was virus pneumonia free, there was certainly quite a substantial improvement; on the other hand, he knew herds which took no step to get rid of virus pneumonia which showed as good performances as specific pathogen-free herds.

Until the effect on performance was known, and how long the improved conditions could be maintained, it should be left to the research workers to solve the problem rather than to commercialise it in the way that the Americans had done and some people here were trying to do.

He had been struck by the example already quoted that 10 years ago there was a very similar move in the United States as far as artificial rearing of pigs was concerned. There was terrific enthusiasm, a little laboratory evidence to show that it could be done, commercial exploitation on a terrific scale and under veterinary supervision. Within 2 or 3 years, when it was followed in this country, it had to be admitted that it was a failure. He still believed there was a potential in artificial rearing and hoped that the day might come when that routine might be adopted for practical purposes but he suggested that, both in the case of artificial rearing and in the minimal disease field, a lot more research was needed and more factual evidence wanted before one took the jump as had been done on several occasions before, only to find there was no water in the pool.

Dr. N. Underdahl said that it appeared that a lot of the questions were probably directed at him. Referring to the slide shown by Dr. Betts on 2 years of the American programme, he said that he himself could have put on a slide for 3 complete years. He then showed a slide referring to 37 animals taken in 1957 and placed out on to a farm. There were, in the Nebraska Association, now 60 farms that had been repopulated from the original 37, with the exception that new boar lines had been brought in to add to the stock. At present, the average in almost 5,000 pigs that had been farrowed and raised was a 154-day weight of 201 lb. From the spring farrow this year, about one-third of the pigs had been weighed out and the average was 213 lb.

With regard to problems concerning certification or accreditation of herds, there were 3 farrows out of 74 in the past 3 years that had not been accredited. With 2 farrows, it was thought that virus pneumonia was in the herd. That farm had been followed along and in the last farrow in the spring, the pigs were free of pneumonia. It was not possible to isolate anything from the herd, and it was felt that the condition had been due to a combination of another viral agent with heavy *Ascaris* migration.

The third farrow that was not accredited was one which looked as if it had atrophic rhinitis; 6 pigs were involved in 120 animals in one farrow and 7 in 140 in the second

farrow. It looked as if the condition was genetic in origin. All the other snouts in the herd appeared normal.

The thing that kept pigs from being accredited or certified was performance. A fairly high standard had been set of 155 lb. average for the herd at 140 days. That was set lower than he would have liked because some of the pure-bred people had a hard time achieving that, but it was still higher than the average American farmer obtained. In the 74 farrows in the past 3 years, 56, or about 76 per cent. of the animals had passed the performance standard of 155 lb. In the herds that did not pass nutritional problems were primarily to blame. The farmers had not been given instructions on how to feed their animals. The animals had been cared for much as the farmers had done in the past.

American feeding methods were entirely different from the British. He had been at a farm the day before looking at the prepared ration and feeding methods. They were entirely different from the way the pigs were fed in America. In America some fed protein supplement to the basic maize diet free choice, others fed supplement by hand and some would not feed supplement at all. All three methods were used on farms in the Nebraska SPF programme.

Regarding the way Nebraska farmers in the programme were classified, from observing them over the last 3 years, on the American standards, 10 of the 30 farmers were thought to be poor managers; 16 were classified as average and 4 as good.

In the States of Iowa and Minnesota, certificates and medals were given to "star" farmers in pig production. In Iowa last fall, 25 farmers received medals and their pigs averaged 168 lb. per pig at 154 days. In Minnesota, 25 farmers averaged 168¼ lb. per pig, so the "star" farmers in the two States were doing approximately the same. It was instructive to compare the performance of pigs in the specific pathogen-free programme under comparatively poor conditions of management with the performance of these ordinary pigs under better conditions; the better farmers had been outdone by almost 40 lb. at 154 days.

Dr. Goodwin asked whether the pigs that were 201 lb. at 154 days were on *ad lib.* feeding.

Dr. Underdahl replied that they were as were the vast majority of American pigs.

Dr. Goodwin asked how much of the improved performance did Dr. Underdahl think was due to the reduction of chronic respiratory disease, which was the main reason why the American programme had been started, and how much was due to other pig diseases. Furthermore, how much of the improved performance did he ascribe to atrophic rhinitis and/or the disease known to Dr. Underdahl as "virus pneumonia."

Dr. Underdahl said that from experience with some of the herds and with the herd at the University, atrophic rhinitis did not appear to affect the growth rate of the pig. The first pigs that went to market in the University herd, before they were cleaned up, had as high a percentage of pigs involved with serious lesions of atrophic rhinitis as the last pigs that went to market 40 to 50 days later. It was felt that most of the benefit gained from repopulating the herd had been in lifting virus pneumonia from it.

Dr. A. B. Paterson (Weybridge) asked if there was any evidence for transmission of viruses from mother to foetus as occurred in German measles of man or swine fever of the pig. In cytomegalic inclusion disease in the rat or guinea-pig, virus was believed to go from mother to foetus. In general, foetal tissues were an excellent medium for the growth of viruses *in vitro* and the foetus might well be a predilection site *in vivo*. In the production of disease-free pigs by hysterectomy the assumption was made that certain viruses did not infect the foetus. Was this indeed true?

Dr. Betts, in answering Mr. McCrae's questions commented on the results of the work study of the hysterectomy operation and went on to the question of methods other than hysterectomy which could be used for obtaining pigs from the uterus.

Obviously it would help preserve genetic material if a valuable sow could be saved. With his colleagues he was thinking in terms of producing pigs by hysterotomy but these were intended to be "germ-free" rather than "pathogen-free." The pigs would be reared in sterile inflated plastic "balloons." The problem was not only to obtain pigs in a sterile way but also to transfer them to the "rearing balloon" without any bacterial contamination whatsoever. They were investigating the possibilities of sticking an inflated plastic balloon to the abdomen of an anaesthetised sow and actually operating through the wall of the balloon so the piglets had no contact with the outside air.

One other way which had been suggested for removing pigs from the uterus was *via* a sterile flexible plastic tube inserted through the cervix shortly before farrowing.

Mr. McCrae had mentioned taking pigs by hysterectomy and rearing them on foster mothers. The disadvantage of this procedure was that the pigs so reared would only be free from the same diseases as the foster mother.

At Cambridge there had been no peculiarities of behaviour such as difficulty with pigs urinating or defaecating. One odd thing had been noticed, however. It was necessary to put pigs in individual isolators to prevent them sucking the umbilical cords of other pigs and bleeding each other to death. Thus, when they were taken from the incubators they had not seen other pigs and were often very frightened of their litter mates.

On the question of differences in structure it should perhaps be pointed out that the pigs described were certainly not "germ-free." Bacteria could be detected in the faeces at 4 to 7 days as a rule. In "pathogen-free" pigs no real differences in structure had been noticed. One had the impression that the wall of the gut was a little thinner than usual but this was only an impression.

Terminology was a difficult matter and people had been thinking about it since the first "germ-free" animals had been produced early in the century. No satisfactory terminology had yet been devised so it was unlikely that there would be a quick solution to the problem.

Mr. McCrae had mentioned gamma globulin. Some "germ-free" pigs had been produced in at least 2 centres in the United States but as far as he knew no work had been done on the gamma globulin content of these pigs. As far as "pathogen-free" pigs were concerned, work done using dead antigens in the United States had shown that there was no marked response until the pigs were 6 to 8 weeks of age. However, the inoculation of living viral antigens at Cambridge had given rise to an antibody response at 3 weeks of age. It was worth bearing in mind that since "pathogen-free" pigs were not free from bacteria they might develop some gamma globulin in response to non-pathogenic bacteria.

The diet that was used for feeding the young pigs was made up without penicillin. To date no serious nutritional deficiencies had been encountered. But this might be due to the fact that the little pigs were used for experiments before they were very old.

On the point concerning the sacrifice of the sow and the consequent loss of genetic material; hysterotomy was, as yet, not generally applicable but many of the objections to hysterectomy could be overcome by performing hysterectomy on old sows at, say, the fifth litter. This would have two advantages. By the time the fifth litter had been reached the sow's performance would be known and, moreover, the sow would not be of very great economic value. This made the whole procedure cheaper.

With regard to the hysterectomy procedure being outside the Veterinary Surgeons Act, it was a fine point whether the animal was dead or not at the time of operation. The operation took place during the slaughtering process and there seemed no reason why the procedure could not be modified so that one could be sure that the animal was dead at the crucial time. If the animal was dead it was difficult to see how the procedure could be regarded as being within the Veterinary Surgeons Act.

Finally Mr. McCrae had referred to the importance of the comparison of performance of different types of pigs. This was certainly desirable and a great deal more information was necessary on the effects of various diseases. It would not be easy, however, to plan and to carry out experiments to test these points to everybody's satisfaction.

He was surprised, but pleased, that Dr. Goodwin had changed his mind so much since last year. With regard to pigs dying off during experiments the pigs referred to had, of course, been deliberately infected with a variety

of pathogens. The highest mortality amongst "pathogen-free" pigs was during the first 7 days of life. Once they were more than 7 days old there was no real problem and the mortality rate was very low.

He agreed with Dr. Goodwin that results from the United States could not be transferred directly to this country. But in trying to compare results to be obtained on farms in this country with those in the United States it was important to see that the pigs were produced in the same way and were of the same health status as in the U.S.A. Dr. Goodwin in referring to his associated company had not described the conditions under which his pigs were being produced; whether procedures were being followed to keep them free from as many diseases as possible or whether the interest was simply in getting them free from virus pneumonia. If it was the latter, he could see no valid objection to mixing virus-pneumonia-free pigs and "hysterectomy-produced" pigs of that status on the same farm: but it seemed to be an odd thing to do to take pigs, over which a lot of trouble had been taken to get them free from as many diseases as possible, and mix them with conventional pigs. That did not seem to be exploiting the technique to its maximum.

Doubts had been cast on whether herds could be kept free from a variety of diseases. The figures quoted by Dr. Underdahl suggested that they could be—unless one considered that American farmers were better managers than British farmers and were more amenable to education. He would have thought that with the rather different system of keeping pigs, particularly with the greater tendency to keep pigs indoors in an enclosed environment the chances of keeping British pigs free from a number of diseases would be greater.

The suggested licensing system for primary production centres would not prevent in any way a veterinary surgeon carrying out what procedures he thought applicable to any particular disease situation on any farm. The development of a licensing system, or any other system of independent control over the large commercial centres, was so that a farmer buying pigs from such a centre would know that he was getting animals which were free from as many diseases as possible. If there were no controls at all and the centres were not under veterinary supervision the farmer would have no protection and would be wide open to exploitation.

Dr. Braude had raised the question of how long pigs would remain free from disease. At present this could not be answered. Pigs were first placed on Nebraska farms 4 or 5 years ago. The results quoted by Dr. Underdahl covered the past 3 years and showed that the improved performance was still being maintained.

The problem could be approached in a slightly theoretical way. On an average farm, given a reasonably intelligent farmer, there seemed no theoretical reason why the herd should not remain free from virus pneumonia, from mange and possibly some other diseases. On the other hand in a new controlled-environment house, if the pigman put on coveralls when he arrived in the morning, pelleted foods were fed and other precautions taken, it could reasonably be expected that a wide variety of diseases might be kept out and that the build-up of disease would occur more slowly. How slowly he had no idea. At some stage it might be economically justifiable to repopulate again. The answers to these questions would not be forthcoming for several years after swine repopulation had become widespread.

The effect of rhinitis on performance had been dealt with by Dr. Underdahl.

Dr. Paterson had asked about agents passing the placenta. Obviously it was not possible to say what would not pass the placenta under any conditions. It was known that swine fever virus could. The virus usually killed a high proportion of the pigs *in utero* while the others were usually oedematous so the condition should be noticed. *Eperythrozoa* could pass through but there was probably not much need to worry about that. At Cambridge no evidence had yet been found of cytopathogenic viruses passing through. Last year he had seen the manuscript of a book from the Harvard Medical School reviewing the permeability of human and animal placentae to infective agents. This included the placenta of the pig. According to this review the number of agents proved to pass the placenta of mammals was remarkably small.

Dr. Braude asked if Dr. Betts could be more specific about what diseases he thought his procedure would eliminate. Was it only virus pneumonia and rhinitis? Mange he himself considered of no importance because there were simpler methods for its elimination. What other diseases did he bring into the orbit?

Dr. Betts said that he did not yet know enough about pig diseases to answer that but it would be surprising if some other diseases could not be kept out.

It would be virtually impossible to keep out indefinitely from the average herd diseases passed by faecal contamination since they could be carried on boots, by birds or by rats. This might not apply to controlled-environment houses.

In general it was the airborne infections that could reasonably be expected to be kept out, apart from any that might transfer from man to pig.

Mr. J. A. Beech (Berkhamsted) asked if any tendency had been noticed for an encouragement of the metabolic type of disease in a pig growing unnaturally rapidly. The question was prompted by the fact that hyperkeratosis is sometimes seen in pigs being fed a growth-promoting factor such as copper or an antibiotic. In these circumstances the condition is said to be due to a relative deficiency of unsaturated fatty acids. The slower growing animal can synthesise sufficient unsaturated fatty acids for its requirements even in the event of dietary insufficiencies.

Dr. Betts said that on this his experience was limited. Most of the pigs produced at Cambridge were used for experiments with infectious diseases and he was not worried too much about nutritional deficiencies. He understood that in Nebraska, some nutritional deficiencies had occurred on farms.

Dr. Underdahl said that many food salesmen had encouraged farmers whose pigs had skin trouble to increase the calcium. The calcium had been increased and the phosphorus had remained the same. Now, the calcium was being increased but the ratio of one part calcium to 1.2 of phosphorus was being maintained. That had helped the situation. In some cases, pigs had been getting up to 13 parts of calcium to one of phosphorus.

As far as the skin condition caused by zinc deficiency was concerned, last month one of the specific pathogen-free herds taken by hysterectomy had come down with that condition. Two infected ones had been brought into the laboratory and one was put in contact with a pig taken by hysterectomy. After three days that pig had the condition, dying on the seventh day. He had transferred the condition into hysterectomy pigs 6 times. The cause seemed to be a small virus which caused ulcers on the skin, on the tongue and round the lips. The virus alone did not actually kill a pig but caused lesions. In conjunction with bacteria which he had not been able to classify when he left, it was a serious disease and killed pigs in 5 to 7 days.

The Chairman thanked Dr. Betts for his paper and for answering the questions so well. He also thanked Mr. McCrae for opening the discussion.

TOXIC CHEMICALS IN AGRICULTURE

The Report of the Research Study Group on Toxic Chemicals in Agriculture and Food Storage was published last Wednesday. This group of scientists has made a thorough survey of the considerable amount of research now going on into the use of toxic chemicals in agriculture and food storage, with particular reference to protecting human beings, farm animals, bees and the different forms of wild life against possible hazards.

The conclusions of the Report are that protective measures now in force are generally successful, but it affirms and spells out the need for more fundamental and applied research into various problems arising in this field.

A Toxic Factor in Brazilian Groundnut Causing Liver Damage in Pigs

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SUMMARY.—An outbreak of disease in pigs involving liver damage of a specific nature is described. The relationship of the feeding of groundnut meal of Brazilian origin to this condition is discussed, and the production of the condition in experimental pigs described.

Introduction

STEVENS, Saunders, Spence and Newnham (1960) reported heavy losses in turkey poults during the early summer of 1960 from a previously unrecognised disease, the nature of which had not been established. Similar losses were subsequently reported by other workers. Later in the summer of 1960, suspicion was directed at groundnut meal of Brazilian origin, this being a foodstuff common to all the outbreaks (Blount, 1961). Subsequently, Dr. Allcroft and colleagues extracted a toxic factor from Brazilian groundnut meal (Allcroft, Carnaghan, Sergeant & O'Kelly, 1961).

In the summer of 1960, it was thought that this meal was not toxic to other species of animals, but further experience has shown that it is. The object of this paper is to describe an outbreak of poisoning in pigs following the feeding of this meal, to refer to other suspected cases, and to outline the experimental production of the condition in this species.

History

The herd first concerned consisted of 125 breeding sows and gilts, principally Landrace × Landrace/Wessex Saddleback but with some pure-bred Wessex Saddleback, together with followers to pork weight.

The sows farrowed and reared their litters on grass in an exposed position on the Chiltern Hills. Wooden arks were provided for shelter. Starter pellets were available to sucking pigs from, at the latest, 2 weeks old. Sows were mated in groups to farrow within a period of 3 weeks and the sows and litters mixed freely during the suckling period. No separate identification within the group was possible, so that the age difference of the sucking pigs within the group might be as much as 3 weeks. The age of pigs throughout this paper will be given as the group average age.

* Received for publication July 18th, 1961.

Trouble was first seen in a group of 430 pigs at 9 weeks old. Of this group, 300 of the best pigs had been transferred over one week previously to another farm where the conditions of feeding and management were different. The remaining 130 continued on starter pellets for a further 10 to 14 days. Disease was first seen in the latter sub-group on September 7th, 1960, when 4 pigs were found dead and 4 more were sick, dying later that day. The following day a further 22 pigs were sick, all showing jaundice and extreme apathy. All the pigs of the group were brought indoors and kept housed thereafter. Most of the group showed poor appetite and growth and a further 27 died during the next 2 months. Of the 300 pigs moved to another premises, only 2 showed jaundice and apathy and died, one on the 7th, the other on September 9th. The remainder of this group fattened normally.

A similar condition appeared in a group of 404 pigs, this being the progeny of the next group of sows to farrow. Deaths commenced at 8 weeks old and 71 pigs died during a period of 5 weeks. The remainder did poorly and made unsatisfactory carcases.

Two subsequent groups of pigs, farrowed 3 and 4 weeks later, did not show the typical clinical syndrome, but development of the pigs in these groups was poor, and 1 animal slaughtered at 12 weeks had mild liver lesions of the type described below, and which are regarded as typical of the condition. In retrospect, it is probable that these 2 groups only received food containing Brazilian groundnut meal for about 3 weeks.

Several of the dams in all 4 groups showed inappetence, particularly just after farrowing, together with poor milk production and a disinclination to eat anything except grass. These signs were seen in adults on several other farms where food containing Brazilian groundnut meal was known to be fed. A gilt which was sacrificed, and a pork-weight pig which died naturally, both from the original farm, showed typical liver lesions of varying severity.

Up to August, 1961, there had been no obvious effect on the breeding performance of sows which were involved in this episode.

Brazilian groundnut meal was included in the starter pellets at 17½ per cent. of the ration and in the sow and weaner meal at 8¾ per cent.

R. M. LOOSMORE & J. D. J. HARDING.—A TOXIC FACTOR IN BRAZILIAN GROUNDNUT CAUSING LIVER DAMAGE IN PIGS

FIG. 1.—Liver. Enlarged parenchymal nucleus with big nucleolus. H.E. × 675 approx.

FIG. 2.—Liver. Proliferating ductules (indicated by arrows). In the actual section these are more obvious, as they are more basophilic than the parenchymal cells. H.E. × 312 approx.

FIG. 3.—Liver. "Subacute" case. From the septum crossing the bottom right corner, fine pericellular strands of collagen (indicated by arrows) enter the lobule. The centre of the lobule lies towards the top left corner. Picro-Masson. × 312 approx.

FIG. 4.—Liver. "Chronic" case. Narrow bands of fibrous tissue connect the septum (top) with the centrilobular vein (bottom centre). Picro-Masson. × 125 approx.

The type of groundnut meal used in these compounds was changed in the middle of the episode from extracted meal to expeller meal. The pattern of deaths suggest that there was no difference in toxicity between meal prepared by either process.

Morbid Anatomy

The carcases showed generalised jaundice and the most marked lesion was discoloration of the liver, the colour varying from off-white to bright orange. The blood was still fluid. Gross haemorrhage was present in many parts of the body, most commonly in subcutaneous tissues and under the mesentery. Ulceration of the oesophageal zone of the stomach was present in some cases.

Histopathology

Histological examinations were made on the following tissues from pigs drawn from various groups between September 18th, 1960, and February 8th, 1961:— 23 samples of liver, 11 samples of kidney, 5 samples of heart, 2 samples of intestines and one sample of lung. In addition, all the major organs from 2 pigs were studied microscopically. In the livers, lesions which appeared to represent consecutive stages of a single disease process were observed in 9 pigs. The other organs did not reveal any clear pattern of changes.

The liver lesions might be divided into 3 stages, acute, subacute and chronic.

In the acute type the normal "cord" pattern of the lobule was broken up. The parenchymal cells varied in shape and size, and a number contained greatly enlarged nuclei, often with prominent nucleoli (Fig. 1). Bile casts were sometimes present. In paraffin-embedded sections stained by haematoxylin and eosin, the parenchymal cells showed a moderate number of coarse and fine vacuoles, but in comparable frozen sections stained by Scharlach R, a spectacular quantity of lipid was revealed. Around the edges of the lobules, and in lesser numbers in their depth, cells rather more basophilic than the parenchymal cell, with more vesicular nuclei and less prominent nucleoli, formed plates, rosettes and incomplete tubes (Fig. 2). This probably represents rather imperfect "ductule proliferation," and although these cells resemble bile duct epithelium more than parenchymal cells, they appeared in places to be continuous with groups of the latter. The probable origin of the cells of proliferated ductules has been discussed by Schaffner and Popper (1961).

When sections were stained by Gordon and Sweet's modification of Foot's method for reticulin and by a picro-Masson method for collagen, fine strands of reticulin and collagen could be observed, extending from both the portal triads and the interportal segments of the septa into the substance of the lobule, separating and isolating small groups of parenchymal cells (Fig. 3).

In the cases interpreted as subacute, this process of pericellular fibrosis was more advanced, and there was sometimes an increase in collagen around the central veins, though their lumina remained patent.

In some pigs which had belonged to groups in which acute disease had occurred, but which had survived to an age of 14 weeks or more, lesions interpreted as chronic were seen. In these livers fatty change and marked enlargement of nuclei were not detected; the septa were only slightly thickened, but the lobules were dissected by narrow bands of fibrous tissue running from the septa and portal triads to the central veins, and in some cases the central vein appeared to be reduplicated (Fig. 4).

In no specimen was true veno-occlusion seen.

Experimental Evidence

Two 4-week-old pigs were fed the starter pellets concerned in the outbreak and 5 others were fed a specially compounded ration containing 20 per cent. Brazilian groundnut. Is pigs from both groups, which died or were killed after 4 to 6 weeks, there were liver lesions identical in type with those described above as "acute," and "subacute." Control pigs fed proprietary starter pellets* in the first case, or a ration containing 20 per cent. Nigerian groundnut meal in the second case, did not develop liver lesions.

Attempts to reproduce the "chronic" lesion are in progress, and the whole series of experiments will be reported in detail when complete.

Discussion

When the outbreak occurred, the possible involvement of Brazilian groundnut meal similar to that used and suspected in turkeys was considered, but its presence in the meal was not confirmed for some time. It was known from a previous investigation into copper poisoning in lambs on this farm that the pasture copper content had been high, and in view of the similarity of the gross *post-mortem* lesions to those of experimental copper poisoning in pigs (Allen & Harding, 1961), the possibility of such poisoning was pursued. In fact, analyses showed the liver copper contents to be within or below the expected normal limits. Furthermore, there was now no abnormal copper content in pasture herbage samples. Extensive examinations for microbiological causes and for inorganic poisons produced no results. Once the presence of Brazilian groundnut meal had been determined, it was possible to suggest an explanation for certain points in the clinical history. It seemed probable that only very young pigs were sufficiently susceptible to develop typical clinical signs; in older pigs the signs apparently accompanying ingestion of this substance were not specific. These non-specific signs of inappetence were seen in sows on at least 5 other farms where the sow and weaner meal from the same miller was fed, but no young pigs of the apparently susceptible age were on these farms during the time Brazilian groundnut meal was included in the starter pellets. On one other farm using the same starter pellets containing Brazilian groundnut meal a few deaths occurred in weaners and typical liver lesions were found, but the number of pigs at risk was small.

It appeared from field evidence that piglets had to ingest the substance for at least 6 weeks before showing clinical signs and this may explain the infre-

* "Amvilac," Glaxo Laboratories Ltd.

quency with which this condition occurs over the country as a whole.

The outbreak described drew attention to the condition because of the large number of pigs of susceptible age which were fed on the meal. Other factors which may have contributed to high mortality on these premises were the exposed position of the farm; a period of unseasonably cold weather; the higher consumption of starter pellets under the outdoor system; the practice of continuing to feed starter pellets for 2 weeks after weaning; and possibly the incidence of severe inclusion body rhinitis in this herd as a debilitating factor. It should be borne in mind that experience with these and other batches of Brazilian groundnut meal suggests that different samples can vary considerably in toxicity.

The gross and microscopic lesions described above bear some resemblance to those of experimental copper poisoning. In both diseases there is generalised jaundice, the livers are yellow to orange in colour and the oesophageal zone of the stomach is often ulcerated. However, in copper poisoning pulmonary oedema is conspicuous, and the intestinal contents are bloodstained even in the absence of gastric ulceration. Neither of these lesions were seen in the cases described here. In both diseases histological examination of the liver reveals disorganisation of the normal cord structure and enlarged parenchymal nuclei, but ductule proliferation, steatosis and pericellular fibrosis, which were striking in the cases of Brazilian groundnut poisoning, have not been seen in experimental copper poisoning.

The nature of the toxic principle involved is not at present clear and it cannot be assumed with certainty that the poison is confined to Brazilian groundnut meal. Lesions in other species bear a close resemblance to those of ragwort poisoning or seneciosis (Loosmore & Markson, 1961), but a search of the literature did not yield any detailed description of the lesions of seneciosis in pigs, so this aspect cannot be discussed. However, there seems little doubt that some toxic factor in Brazilian groundnut meal was responsible for the clinical signs and lesions encountered in this outbreak of disease.

Acknowledgments.—The authors would like to acknowledge gratefully the help and co-operation received from Mr. W. B. Faull, B.SC., M.R.C.V.S., of Wallingford, from the farmer concerned and from the millers involved. Thanks are due also to the Biochemistry Department at Weybridge, for carrying out all the analytical work.

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SYMPOSIUM ON RADIO PILLS

On October 28th the Bioengineering Society held a symposium under the chairmanship of H. S. Wolff at the M.R.C. Laboratories, Hampstead, London, S.W.3, where papers were presented and discussion promoted among various groups interested in the development of radio pills.

The radio pill or telemetering capsule consists of a minute transducer and radio transmitter the size of an ordinary drug capsule, the radio signal from which may be picked up by a suitable receiver, by means of which permanent recordings may be made on a direct-writing recorder. Depending on construction, pressure, *p*H or temperature can be measured.*

The technique was pioneered by workers in Sweden (Mackay & Jacobson, 1957) and America (Farrar *et al.*, 1957; Farrar & Bernstein, 1958) and developed in these countries, Germany and Britain.

The veterinary research possibilities are great as such pills may be introduced into organs and cavities not available to medical workers.

Papers presented were: "Review of work with radio pills carried out at the Western General Hospital, over the past two years," M. Ridgway, Medical Physics Unit, University of Edinburgh; "The use of radio pills in veterinary research. Modifications required for use in domestic animals," A. F. Munro and A. D. Weaver, University of Glasgow; "A re-usable pressure pill with a metal diaphragm, and clinical results obtained," B. Watson and B. Ross, Medical Physics Department and Department of Surgery, University of Sheffield; "A high sensitivity temperature-sensitive pill," J. Baker, Bioengineering Laboratory, M.R.C.; "A very long life temperature-sensitive pill for implantation," G. B. Horsfall, I.C.I. Ltd.

Among points discussed were the use of serials, localisation of the pill in the body, recovery and sterilisation procedures, interpretation of recordings and aids to data processing, the future of passive pills and commercial aspects.

While likely to prove a useful research tool for physiological and pharmacological investigations, clinical application cannot be foreseen in the immediate future. The price limits widespread usage, as each pill currently costs £10. Should consumption increase considerably this will be much reduced as a result of automation. Discussion revealed that in the medical field the experimental application of such pills was limited, and the greatest advances seem probable in electronic research directed towards greater reliability and accuracy, and increased life and power. Several workers are manufacturing their own pills.

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* Pressure pills have been produced commercially by Solartron Ltd., and shortly *p*H pills will be marketed by E.I. Ltd.

The Nuffield Institute of Comparative Medicine

Conference on Comparative Aspects of Cardiovascular Diseases

We are indebted to Mr. R. N. Fiennes, secretary of the Institute for the following report.

A conference on the comparative aspects of cardiovascular diseases was held at the Zoological Society on November 22nd. The conference was convened by Professor Sir Roy Cameron as Chairman of the Nuffield Institute Committee and its objects were as follows:—

1. To study the existing state of research in the United Kingdom in relation to diseases of the arterial system.
2. To consider what contribution can be made by the Nuffield Institute of Comparative Medicine.
3. To consider in what ways studies on comparative aspects of arterial diseases can be correlated, and in particular how the programme of the World Health Organisation on these diseases could be advanced in this country.

A model of the projected Institute was demonstrated during the course of the conference by the architect, Professor R. Llewelyn Davies, but unfortunately the Institute itself is not likely to be ready for occupation for 18 months to 2 years. It may be wondered, therefore, why the committee considered the present time appropriate to call a conference of this nature. The answer is that, owing to the interest of the veterinary section at the London Zoo in comparative cardiovascular disease, links had been developed with the veterinary public health section of the World Health Organisation and it appeared that action to forward the Organisation's plans required to be taken immediately, and that a great deal could be done in the intervening period until the Institute's own laboratories were ready.

Veterinary representation from this country was arranged by circularisation of all research institutes where it was thought that research on arterial diseases might be in progress. Subsequently, interested members of the profession were invited to a preliminary conference which was held at the Royal Veterinary College on October 10th under the chairmanship of the Principal, Dr. R. E. Glover. At this conference work in progress was reviewed and 5 delegates were nominated to attend the main conference.

The following veterinary scientists attended the conference either as delegates, speakers or invited guests:—

Sir John Ritchie, Dr. R. E. Glover, Dr. E. Cotchin, R. N. Fiennes, Professor W. I. B. Beveridge, Dr. W. P. Blount, A. R. Jennings, R. S. Marshall, O. Graham-Jones, R. S. F. Campbell, J. T. Done, Professor C. W. Ottaway, J. C. Whitney and R. Scarisbrick.

The conference was opened by Sir Solly Zuckerman who welcomed the guests and spoke of his hopes and ambitions for the new Institute. He said that the Zoological Society of London owned the largest collections of captive wild animals in the world, and thus had an unrivalled pool of material for research work which he had long wished to see fully used. Research in progress showed that there was a high incidence of arterial disease in almost all groups of animals, and it was evident that research into its causes and incidence might well throw light on the problem in man and domestic animals. Sir Solly was followed in an outstanding contribution by Dr. Martin Kaplan on "The comparative medical approach in the World Health Organisation to the problem of Atherosclerosis." Dr. Kaplan said that the World Health Organisation was especially interested in human/animal relationships, and considered that comparative studies could make a contribution to both human and veterinary medicine by taking a look at problems in a new context. This approach could well provide important clues to cardiovascular and neoplastic diseases. The essence of such an approach was the relationship of animals to their environment including the epidemiology of chronic disease conditions. It involved an approach to the animal as a complete organism rather than to single organs or systems. Concentration was on naturally-occurring disease processes rather than on disease induced in the laboratory. The Organisation had limited funds, and its design was mainly to promote studies through the goodwill of scientists in different countries. For this purpose attempts were made to form scientific groups in suitable areas, particularly where geographical studies showed a high incidence of the disease in question. In reply to Sir Harold Himsworth who stressed the value of comparative studies he maintained that nature herself provided experiments of higher value than man could devise. Man could make use of nature's experiments by means of geographic pathology.

Dr. Kaplan was followed by Dr. Detweiler who gave a detailed account of the extensive work in progress in the United States. The atherosclerosis problem was approached in six main ways: epidemiological; lipid metabolism; spontaneous atherosclerosis; the relationship of the living organism to its environment; biochemical; behavioural studies, *e.g.* exercise, feeding, etc. Sixteen per cent. of research projects on cardiovascular disease dealt with atherosclerosis or arteriosclerosis. There had been in recent years a considerable expansion of the animal species used in this work, which now included primates, swine, dogs and pigeons. A development of especial interest was in the establishment of regionally-situated primate colonies at which disease problems generally could be studied, in particular cardiovascular disease. For this purpose a high level of financial support was available.

Professor Crawford in another contribution of outstanding merit, illustrated by colour slides, outlined the pathogenesis of atherosclerosis in man, described the theories of causation, and made particular reference in considering the epidemiological aspect to the studies of Professor Morris and his collaborators at the London Hospital. Professor

(Concluded at foot of page overleaf)

Current Literature

ABSTRACTS

Uber Farbanomalien im Augenhintergrund von Haustieren. KAMER (1960). *Schweiz-Arch Tierheilk.* **102.** 501. Translation: Colour Anomalies of the Fundus of the Eye in Domesticated Animals.

The retina was examined by direct vision in 300 horses, 230 cattle, 70 dogs and 30 cats. Histological examination of a small number demonstrated the cause of four observed non-pathological colour anomalies to be due to abnormal distributon of pigment.

(a) Albinismus chorioideae partialis=areas of pigment in the choroid=tapetum coloboma, noted especially in horses (20 cases).

(b) Albinismus chorioideae—diffuse decrease of pigment, in all species.

(c) Excess retinal pigmentation, in horses and cats.

(d) Albinismus retinae partialis=areas of pigment deficiency in the retina=tapetum insulae in horses.

These anomalies are congenital, and do not impair eyesight (5 coloured illustrations).

Uber die Strongyloidose der Kälber. SUPPERER, R., & PFEIFFER, H. (1960). *Wien. tierärztl. Mschr.* **47.** 361. Translation, Strongyloides Infection in Young Calves.

About 35 per cent. of week-old calves in Austria are infected with strongyloides papillosus. The infection is usually mild, and since clinical signs only appear following massive infestations, veterinary help is rarely sought.

A severe infestation is characterised by coughing and cessation of growth. Diarrhoea is sometimes present. Neguvon (a phosphoric ester, Bayer Leverkusen) is very effective at a dosage of 90 mg. per kg. and can be used in weakly calves at 75 mg. per kg., whereby the majority of the parasites are eliminated.

A. D. W.

Experimental Treatment of Ovine Vibriosis. RYFF, J. F., & BREEN, HAROLD (1961). *Am. Vet. Med. Ass. J.* **139.** 665.

A trial over a 4-year period involving 3,143 ewes in flocks where vibrionic abortion was occurring showed that intramuscular injections of streptomycin, oxytetracycline and a repository streptomycin, or sulphabromomethazine or oxytetracycline given orally

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The Nuffield Institute of Comparative Medicine.—*Concluded.*

Crawford was followed by Dr. French who described the work on pigs in progress at Oxford by the research team under Sir Howard Florey. Professor Beveridge then outlined the considerable amount of work in progress at veterinary institutions, of which a review had been made at the preliminary conference on October 10th. The final contribution was made by Dr. Finlayson and Dr. Symons on their studies of the atherosclerosis problem in wild animals, made in collaboration with the writer at the London Zoo. This paper, together with those of Dr. French and Professor Beveridge, underlined forcibly the contribution which might be made by a species-wide study of the natural history of the problem.

Often with conferences of this nature the greatest value is derived from the personal contacts which are established between workers on similar subjects. New relationships are developed and new ideas and approaches are suggested. It surprised many to learn that the comparative anatomy of the aorta in different animals is virtually unknown. The haemodynamics of cardiovascular disease has been little studied and there is no sure information as to whether structural and histological differences in different parts of the aorta may contribute to the sites where lesions develop. R. S. F. Campbell of the Glasgow Veterinary School carried this line of argument further, when he pointed the need for research into the physiology and metabolism of the arterial wall and its relationship to the activity of steroids and oestrogens. In his introduction to the Discussion, Dr. Fejfar stressed also that knowledge was woefully lacking in the field of pathogenesis, and that in order to ascribe certain causes to certain lesions it is necessary first that the lesions shall be classified on a standard basis. Are the lesions in animals similar to those in man and can the lesions in the one indicate a similar cause in the other?

Sir Howard Florey in a deliberately provocative introductory address attacked the epidemiological approach and *post-mortem* studies as the main weapon of research. He met a worthy opponent in Dr. Kaplan who adequately defended the approach developed by the World Health Organisation.

The account given does not, for reasons of space, include many valuable contributions made by other speakers both veterinary and medical. This was a significant day for the new Nuffield Institute of Comparative Medicine and one which will give satisfaction to members of the veterinary profession. Dr. Kaplan in his opening paper expressed the outlook of this Institute, which coincides with that of the World Health Organisation. The new Institute regards medicine as neither human nor veterinary, but as a branch of biology to which all sections of biological science and of physics and chemistry can contribute. The common meeting ground which was developed between the two great branches of the medical profession exactly fulfils the ideas which have inspired the foundation of the Institute and which were ably summarised by the Director of the Nuffield Foundation, Mr. L. Farrer Brown, in his closing address of thanks to the participants and speakers.

After the conference those present were able to see a demonstration of a cardiac analogue devised and constructed by Group Captain J. Malcolm, O.B.E., B.SC., M.B., CH.B., L.R.C.P., F.R.C.S., which showed some of the dynamic stresses and strains developed in a system of closed elastic tubes where the flow of liquid is subject to periodic impedance.

all helped to control abortion. The most consistently good results followed the use of repository streptomycin. G. B. S. H.

Helminth Infestation, a Complicating Factor in Nutritional and Grazing Experiments. CAMPBELL, J. ALLEN, & FIELD, A. C. A paper delivered to the International Grassland Congress, 1960. Section 13B.

The authors stress the importance of internal parasites in experiments designed to study nutrition and management. They point out that in the last few years the majority of papers devoted to these aspects of sheep husbandry have taken very little cognisance of the importance of parasites. They stress the individual variation of the reaction of sheep to parasites and mention the fact that parasites are not distributed in a normal manner; they also emphasise the necessity for appropriate measurement and statistical analysis. The authors quote numerous examples where the nourishment of the host is an important factor in controlling the helminth burden under general conditions; however, they also give instances where there is obviously a need for minerals and trace elements by the parasite. This is particularly true with cobalt. In addition to these complicating factors, they also point out that the strain or species of parasite is of importance. Amongst the other factors which the authors consider should be taken into consideration is that of larval latency. They are undecided as to the importance of this but they stress that it should be taken into account. They reach the conclusion that worm-free animals should be used for various experiments but maintain that the production of worm-free animals is an expensive, difficult and "quite unrealistic procedure, except in very special circumstances." The abstractor would not agree with this conclusion in so far that he does not consider that this is an unrealistic procedure. The production of germ-free animals should be brought to mind here. The authors end by appealing for a closer liaison between the people of various disciplines.

Some Factors Affecting the Significance of Internal Parasites in the Utilisation of Grass by Sheep. SPEDDING, C. R. W., BROWN, D. H., & LARGE, R. E. (Grassland Congress as above.)

The authors experimentally confirm the well-known phenomenon that on hill farms single lambs are less affected by adverse conditions than twin lambs. As with the authors of the first paper, they emphasise the necessity of considering the parasite burden of animals during nutritional experiments. Particular attention is drawn to the fact that management of a flock or a group of animals must be modified according to the stocking rate and according to the lambing rate.

The Control of Nematodirus Disease by Grassland Management. BLACK, W. J. M. (Grassland Congress as above.)

Black discusses the control of *Nematodirus* infection in lambs and maintains that this can be done without recourse to "an expensive anthelmintic." Black deals first of all with the seasonal variation in the emergence of larvae, and ascribes the appearance of clinical Nematodiriasis to a delayed or cold spring. He discusses the benefits of resting pastures and produces evidence of its success. He further considers the resting of pastures for a limited period during the time of larval emergence but concludes that such a procedure is unwise in the absence of detailed information regarding the parasite level on that pasture. The importance of mixed grazing and the utilisation of herbage by cattle is demonstrated to be beneficial for the control of *Nematodirus* disease. The abstractor is of the opinion that though such husbandry methods can be shown to be applicable, the use of the efficient anthelmintic of the bephinium has quite definite and practical applications.

Glucose Utilisation in Sheep. ANNISON, E. F., & WHITE, R. R. (1961). *Biochem. J.* **80.** 162.

Glucose utilisation in fed and in starved sheep was measured by isotope dilution; and values are given for the utilisation rates and body glucose pools. The results indicated the central importance of glucose in sheep metabolism, the utilisation rates in starved sheep—calculated in terms of metabolic bodyweight —being 75 per cent. of those reported for starved dogs.

Rough estimates of the contribution of glucose to over-all oxidative metabolism were obtained by a comparison of the specific activities of plasma glucose and blood CO_2. The results suggested that in fed and in starved animals 2 to 23 per cent. and 11 to 19 per per cent. respectively of blood CO_2 was derived from glucose. Under glucose load this value rose to about 30 per cent.

The Effect of Glucose and Acetate on Milk Secretion by Perfused Goat Udder. HARDWICK, D. C., LINZELL, J. L., & PRICE, S. M. (1961). *Biochem. J.* **80.** 37.

The authors have perfused isolated goat udders and studied the influence of acetate and glucose on respiration and on milk production and composition.

In glands receiving glucose plus acetate, the oxygen uptake and respiratory quotients were similar to those of udders of conscious goats in declining lactation. Milk of reasonably normal composition was secreted for 12 hours at about 50 per cent. of the initial (pre-experimental) level.

Glands given glucose only had a lower oxygen uptake and R.Q. below 1. The milk yield fell to about 40 per cent., and the milk fat to below 20 per cent. of the initial level.

With acetate only, the oxygen uptake was equal to that with glucose, but the R.Q. higher than with glucose plus acetate: but milk secretion fell to very low levels and was restored by adding sufficient glucose, but not by small quantities of glucose or fumarate.

The results confirm that acetate and glucose form milk fat and lactose respectively, but show that in addition glucose is essential for secretion of fluid.

The authors suggest that secretion of fluid, lactose, protein, and fat, are to some extent independent processes. The relationship of these findings to pathways of glucose metabolism is discussed. D.E.K.

Variation in Oestral Cycles of Holstein-Friesian Cattle. MARES, S. E., MENGE, A. C., TYLER, W. J., & CASIDA, L. E. (1961). *J. Dairy Sci.* **44.** 897.

It is generally accepted that oestrus occurs regularly throughout the year in the cow, and that there is a 21 day oestral cycle. However, there are variations and records were made in a herd maintained for experimental purposes. The herd consisted of 6 sire lines (all the descendants of particular foundation sires through the male parents), and 4 systems of matings were practised (outbred animal from an outbred dam, outbred animal from an inbred dam, inbred animal from an outbred dam, and inbred animal from an inbred dam).

The oestral cycles in heifers were studied from the time an animal became one year of age until the first insemination at the first oestrus after 15 months of age. The return intervals were calculated for those animals which did return, and in which no evidence of conception could be found.

The mean lengths of 766 oestral cycles and 191 return intervals from 221 heifers showed lengths of 22.3 days for oestral cycles and 25.3 days for return intervals.

It was found that the summer and spring born heifers had the longest cycles, 25.0 and 25.2 days, whereas the winter and autumn born heifers averaged 22.2 and 20.9 days respectively.

The effect of breeding was that daughters of inbred dams had the longest mean cycle length, 24.9 days for the outbred daughters, and 25.6 days for the inbred, while daughters of outbred dams averaged 20.6 days for those that were outbred and 22.2 days for those that were inbred. J.O.L.K.

Zur Anwendung der Perkutanen Osteosynthese am Metacarpus eines Rindes. TEUSCHER, R. (1961). *Berl. Münch. tierärztl. Wschr.* **74.** 31. Translated title, Percutaneous Osteosynthesis in the Metacarpus of a cow.

A four-year-old cow suffered a simple diagonal splinter fracture of the left metacarpus with slight overriding. Treatment was under general and local anaesthesia whereby five 0.7 cm. diameter steel pins were inserted transversely. External fixation was initially synthetic suture material, later by rapid-hardening fibre-glass. Treatment was a failure as a result of purulent synovitis of the deep flexor tendon sheath, osteomyelitis and periostitis. These complications are discussed with regard to future treatment of such cases (4 photographs).

Eine Behandlungsmöglichkeit von Frakturen Langer Röhrenknochen des Rindes. WINTZER, H. J. (1961). *Dtsch. tierärztl. Wschr.* **68.** 226. Translated title, A Method for the Treatment of Long Bone Fractures in Cattle.

Using a modified Thomas splint, author healed 11/12 humeral, 2/2 radial, 2/3 femoral and 4/4 tibial fractures in cattle. This total of 21 cases was selected from 54 bovine fractures received at the Utrecht cattle clinic. The majority of patients so treated were under 2 years old, and the splint was usually kept in place for 4 to 6 weeks. Animals were found quickly to become accustomed to the apparatus, could move and also stand up without difficulty. (10 illustrations.) A. D. W.

The Excretion of Mercaptomerin and its Diuretic Effect Modified by Bromcresol Green and Probenecid. CAMPBELL, DAG E. S. (1959). *Acta pharm. tox., Kbh.* **16.** 151.

The aim of the work described in this and the following papers was to investigate the mode of action of certain mercurial diurectics. The fowl was used in these experiments because it possesses a portal circulation to the renal tubules; and an excess excretion from one kidney, after injecting into the leg veins of the same side, can be attributed to tubular secretion. Urinary mercaptomerin (expressed as Hg) was measured in terms of percentage of the injected dose excreted, and the figures for water diuresis are given in ml. per 20 minutes minus the resting flow.

It was found that mercaptomerin (1.75 mg. Hg. per kg.) was secreted by the tubules, and also gave rise to an excess diuresis on the injected side. The asymmetrical effect was abolished by the prior injection through the wing vein (*i.e.* to both kidneys equally) of either bromcresol green (10 mg. per kg.) or probenecid (50 mg. per kg.). This inhibition was not observed if the above drugs were injected 2 to 3 minutes *after* the mercaptomerin. Probenecid also markedly reduced the total excretion of Hg and the total water loss.

Modification by Bromcresol Green or Probenecid of Urinary Excretion of Sodium, Chloride and Potassium Due to Mercaptomerin. CAMPBELL, DAG E. S. (1960). *Acta pharm. tox., Kbh.* **17.** 137.

It has been shown that mercurial diurectics can bring about a unilateral diuresis in the fowl when injected into the leg veins on one side. In the previous paper, the author has shown that this unilateral diuresis can be abolished by bromcresol green and probenecid. In this paper the above findings are examined in more detail by determining the excretion of sodium, chloride, and potassium, as well as of water.

The diuretic (mercaptomerin, 1.75 mg. Hg per kg.) caused a natriuresis and a chloruresis which was greater on the injected side. Prior injection into the wing vein of bromcresol green (10 mg. per kg.) or probenecid (50 mg. per kg.) abolished this unilateral response, and the probenecid also reduced the total, bilateral diuresis. This inhibition did not occur if the inhibitors were injected 2 to 3 minutes *after* the mercurial. In one experiment, the excretion of injected polyethylene glycol was measured to give an indication of changes in filtrate rate. There were no consistent differences between the 2 kidneys despite a marked unilateral diuresis caused by the mercurial. It was concluded that the mercurial acted solely by altering reabsorption. There were no marked changes in the excretion of potassium following the injection of mercaptomerin either before or after an inhibitor.

H. B.

News and Comment

WORLD VETERINARY CONGRESS AT HANOVER AUGUST 14th TO 21st, 1963

Members of the British veterinary profession are invited to send suggestions for original papers, not previously published, for consideration by the British national committee. Such suggestions should be addressed to the secretary of this committee, W. G. R. Oates, Esq., Royal College of Veterinary Surgeons, College House, Wright's Lane, Kensington.

It should be noted that either the author or co-author of a paper must attend the congress in person to deliver the paper. Suggestions should be in Mr. Oates's hands not later than January 31st, 1962, and those considered suitable will be forwarded to the organising committee for their consideration.

A summary of the provisional programme will be published next week.

IODINE 131 IN MILK

Results are now available for measurements, made by the Agricultural Research Council's Radiobiological Laboratory, of iodine 131 in milk during the week ending November 25th.

The average content of iodine 131 in milk from depots which are sampled daily has continued to decrease. The values during the past 4 weeks are:—

Week	$\mu\mu$c. per litre
October 29th to November 4th ...	127
November 5th to 11th	117
November 12th to 18th	93
November 19th to 25th	74

The average levels of iodine in milk from different regions of the country during the 10 weeks in which sampling has been in progress are shown in Table I.

TABLE I
SUMMARY OF RESULTS OF DAILY AND COUNTRY-WIDE SAMPLING OF MILK FOR IODINE 131 DURING 10 WEEKS SEPTEMBER 16TH TO NOVEMBER 25TH, 1961

Zone	Average contamination $\mu\mu$c. per litre	% of quantity which would give rise to annual average specified by M.R.C.
1. Northern England	100	15
2. North West England	95	14
3. East and East Midland	70	10
4. West Midland	103	15
5. Wales	156	23
6. South and South East England	90	13
7. Mid-western England	98	14
8. Far Western England	127	19
9. Scotland	136	20
10. Northern Ireland	151	22
Country-wide mean	109	16

The Medical Research Council have stated that the acceptable radiation dose would not be exceeded for infants under one year of age, the most susceptible age group of the population, unless the average concentration of iodine 131 in milk rose above 130 $\mu\mu$c. per litre over a period of one year or higher concentrations were maintained for correspondingly shorter periods. This recommendation took into account the likely extent of variations in the contamination of local milk supplies.

Table I shows that the average quantity of iodine 131 which has as yet entered milk in any region of the country does not exceed 23 per cent. of that which would give rise to the annual average specified by the Medical Research Council, the country-wide average being 16 per cent.

In the last statement issued it was concluded that weapons tests which had so far occurred would not cause the annual average specified by the Medical Research Council to be reached in any part of the country. The downward trend since then reinforces this view. Monitoring will be continued so long as an appreciable quantity of iodine 131 is present in milk.

FREEDOM OF BOROUGH FOR MR. ERNEST WARD, J.P.

All his colleagues in the profession will wish to join in congratulating Mr. Ernest Ward, J.P., M.R.C.V.S., who was honoured on November 29th by receiving the Freedom of the Borough of Slough, whose mayor he had been from 1940-45. The ceremony took place at the Slough College of Further Education in the presence of an audience numbering more than 400, which included Lord Astor, Lord and Lady Curzon, Sir Richard Nugent, the President of the R.C.V.S., Mr. L. Guy Anderson, the Registrar, Mr. W. G. R. Oates, Sir Francis Hill, the mayors and town clerks of many neighbouring boroughs, together with county councillors and a host of other dignitaries.

The mayor of Slough, in opening the proceedings, first dwelt upon the history of the conferment of Freedoms such as the company was attending that day, and then told them that, at a council meeting on October 3rd a unanimous Resolution had been passed admitting Mr. Ward as an Honorary Freeman of the Borough "in recognition and appreciation of his distinguished and devoted services to Slough and to the county of Buckingham." He then asked Alderman R. C. Abbott to give an account of Mr. Ward's career.

Having seen active service in the First World War, Mr. Ward studied at the Royal Veterinary College whence he qualified in 1923. He became first an assistant in a Slough practice and later founded the practice of which he is senior partner. He was elected to the then Slough Urban District Council in 1934, and remained a councillor for 27 years. As already mentioned he was elected mayor in 1940. He became a county councillor in 1942, and county alderman in 1950.

Alderman Abbott was followed by Alderman H. Olding who gave the audience further details of Mr. Ward's public career and paid additional tributes to him.

The town clerk then administered the traditional Oath, after taking which Mr. Ward signed the Roll of Honorary Freeman. The mayor presented him with a silver casket containing an illuminated scroll, the latter emblazoned with the Arms of the Borough, and including in its decorated border the Badge of the Royal Flying Corps, the Arms of the Royal College of Veterinary Surgeons and the Shield of the County Arms.

In expressing profound gratitude for the honour accorded him, Mr. Ward referred to his many years of municipal and county office and expressed his indebtedness to his wife for all her help and encouragement in both his professional and public life. He was honoured by the presence of the President of his own Royal College and that of the Registrar, together with so many personal friends, some of them almost of a lifetime's standing.

IMPORTED CHAROLLAIS BULLS

As announced in the press three of the Charollais bulls recently imported by the Ministry developed leptospirosis while in quarantine and have been slaughtered. They were negative to tests for this and other conditions when they left France. The period of quarantine for the remaining bulls is to be extended. The particular organism incriminated is *Leptospira gryppotyphosa*, infection from which has not, the Ministry states, been recorded previously in Britain.

Last Wednesday, the General Secretary of the B.V.A. was invited by the B.B.C. to broadcast on the subject, and he concluded his observations by mentioning the principal points of a press notice which he had caused to be circulated and which read as follows:—

As we understand that the distribution of semen from recently imported Charollais bulls is to commence within the next few weeks, the British Veterinary Association would like to take this opportunity of reiterating the following points which were made in their evidence to the Terrington Committee.

It is impossible to foresee what may be the result of crossing these bulls with our own native cattle but there does seem to be some evidence that the calves resulting from cross breeding with Charollais may give rise to difficulties at calving time owing to the size of the foetus relative to the size of the dam.

From the figures available it would appear that the pure bred Charollais calf is approximately 20 lb. heavier at birth than is the pure bred Friesian and it is well known that Charollais calves are of large conformation at both shoulders and hips.

In particular we would advise that insemination should in the first year be conducted on a moderate scale and should be confined to adult cows where the risk of difficult calvings will be less than would be the case if the semen were used for inseminating maiden heifers.

It is our hope that farmers will also inseminate other cows with similar numbers of our own beef breeds so that a true comparison can be made of this new breed under natural farm conditions.

CLASSIFIED ADVERTISEMENTS

Will readers kindly note that having regard to the Christmas vacation, classified advertisements intended for our December 23rd issue must be received by first post Monday, December 18th. Advertisements intended for December 30th must be received by Wednesday, December 20th.

UNIVERSITY NEWS

Bristol

The first Langford Games were held at the University Field Station, Langford, on November 25th, 1961. On a chilly, but gloriously sunny afternoon a large crowd of staff, students and their friends gathered to watch a feast of entertainment laid on by final year.

The sports were organised on an inter-year basis and teams from second, third, fourth and final years took part. Besides individual events, such as pitching the bale, skittling for a turkey, tossing the gate post and wheel-barrow jousting, a number of team events were organised. The highlights were a mutation of the Eton wall game, won by fourth year, and the tug-of-war, won by the staff; according to many of the students the staff's success was due entirely to the fact that exams were imminent.

Refreshments in the form of hot-dogs, soup and cider were liberally dispensed by the girls of final year.

Mrs. Messervy presented prizes for the individual events and the "International Red Locust Control Fund" Cup went appropriately to final year.

In the evening a highly successful dance was held, and more than one person was heard to say that they hoped the Langford Games would become a regular yearly event.

Dublin

Final Veterinary Examination

(Clinical Medicine, State and Preventive Medicine; Surgery, Obstetrics and Reproductive Diseases)

Pass: Browne, Jane.

R.C.V.S. OBITUARY

We record with regret the deaths of the following members of the profession:—

O'DEA, Alfred Francis, M.V.SC., D.V.S.M., "Belclare," 159, Strand Road, Merrion, Dublin. Graduated from the Royal Veterinary College of Ireland, July 17th, 1909. Registrar of the Veterinary Council of Ireland. Died, November 30th, 1961.

THOMAS, William Howard, Major, late R.A.V.C., of 12, Vint Crescent, Colchester, Essex. Graduated from the Royal Veterinary College, London, July 20th, 1906. Died, aged 76, in the Military Hospital, Colchester, November 24th, 1961.

PERSONAL

Dr. E. L. Taylor, C.B.E., who has for so long enjoyed a distinguished international reputation among veterinary scientists, retired from the service of the Ministry of Agriculture on November 30th.

Births

BATE.—On November 30th, 1961, to Mary, wife of Terence C. Bate, B.V.SC., M.R.C.V.S., of Pillar-box House, Harbury, Leamington Spa, Warwicks., a son, Anthony John.

BUTLER.—On November 8th, to Trudy, wife of M. C. Butler, B.SC., M.R.C.V.S., D.T.V.M. (EDIN.), Veterinary Officer, Machakos, Kenya, a daughter, Rosemary Anne, sister for Peter.

PICKERING.—On November 16th, 1961, to Barbara, wife of Eric C. Pickering, B.SC., B.V.M.S., M.R.C.V.S., of "Viewfield," High Banton, By Kilsyth, Stirlingshire, a second son, Richard John.

COMING EVENTS

December

12th (Tues.). WEST WALES VETERINARY CLUB. Annual General Meeting at the Golden Lion Hotel, Carmarthen, 7.30 p.m.

13th (Wed.). NORTH OF ENGLAND VETERINARY MEDICAL ASSOCIATION. Annual Dinner Dance in aid of the V.V.B.F. at the Banqueting Rooms, Gosforth Park Race Course, Newcastle upon Tyne, 7.30 p.m.

SUSSEX VETERINARY SOCIETY. Meeting at the Old Ship Hotel, Brighton, 6 p.m.

SOCIETY OF PRACTISING VETERINARY SURGEONS. Joint meeting with the Cornwall Veterinary Clinical Club at the Red Lion Hotel, Truro, Cornwall, 7.30 p.m.

14th (Thurs.). SHROPSHIRE VETERINARY CLUB. Meeting at the Oak Hotel, Shelton, Shrewsbury, 8.15 p.m.

15th (Fri.). NORTH OF ENGLAND VETERINARY MEDICAL ASSOCIATION. Meeting in the Agricultural Lecture Theatre, King's College, Newcastle upon Tyne, 7.30 p.m.

January

17th, 18th and 19th (Wed., Thurs. and Fri.). B.V.A. Committee and Council Meetings in London.

ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the date on which disease has been confirmed, followed by the postal address and local authority.

Anthrax

November 28th, 1961. J. Clow, Meikle Whitefield Farm, Burrelton, Couper Angus, Perth (Parish: Cargill). (Cattle.) PERTHSHIRE.

November 28th, 1961. F. Howitt, Pethills Farm, Winkhill, Leek, Staffs. (Parish: Onecote). (Cattle.) STAFFORDSHIRE.

November 28th, 1961. A. Wood, 4, Mitchell Fold, Pott Shrigley, Macclesfield, Cheshire. (Cattle.) CHESHIRE.

December 1st, 1961. Major O. Allhusen, Pinhay, Lyme Regis, Dorset (Parish: Combpyne Rousdon). (Cattle.) DEVONSHIRE.

December 1st, 1961. E. Royle, Blakeley Farm, Mobberley, Knutsford, Cheshire (Parish: Mobberley.) (Cattle.) CHESHIRE.

December 4th, 1961. W. Higgins, Bentleyford Farm, Longnor, Shrewsbury, Salop. (Parish: Acton Burnell). (Cattle.) SHROPSHIRE.

December 4th, 1961. W. J. Soanes, Blackhill Stud Farm, Colgate, Horsham, Sussex (Parish: Lower Beeding). (Horse.) WEST SUSSEX.

December 4th, 1961. W. Whitley, Weaver Park Farm, Winsford, Cheshire (Parish: Darnhall). (Cattle.) CHESHIRE.

Fowl Pest

November 28th, 1961. A. Schmidt, Westfield Bell Bar, Westfield, Hatfield, Herts. HERTFORDSHIRE.

November 28th, 1961. L. Kerridge, 92, Back Street, Garboldisham, Diss, Norfolk. Disease at: Back Street Farm, Garboldisham, Diss, Norfolk. NORFOLK.

November 28th, 1961. A. Aves, Meadows Farm, North Lopham, Diss, Norfolk. NORFOLK.

November 28th, 1961. J. F. Bomford Ltd., Ryden Farm, Charlton, Evesham, Worcs. WORCESTERSHIRE.

November 28th, 1961. J. F. Bomford Ltd., Manor Farm, Pensham, Pershore, Worcs. WORCESTERSHIRE.

November 28th, 1961. J. E. & B. Lebbon Ltd., Beck Farm, Briston, Melton Constable, Norfolk. NORFOLK.

November 28th, 1961. J. Flatman, 2, Cross Green Road, Thelnethan, Diss, Norfolk. WEST SUFFOLK.

November 28th, 1961. A. E. Womack, The Fox Inn, Garboldisham, Diss, Norfolk. WEST SUFFOLK.

November 28th, 1961. J. H. Jones, The Old Rectory, Low Catton, Kexby, York. YORK, EAST RIDING.

November 29th, 1969. G. F. Gill, Church Farm, Hawstead, Bury St. Edmunds, Suffolk. WEST SUFFOLK.

November 29th, 1961. H. A. Peacock, Woodfield Farm, Kentish Lane, Hatfield, Herts. HERTFORDSHIRE.

November 29th, 1961. R. A. Flowerdew, Bush Farm, Denham, Diss, Norfolk. NORFOLK.

November 29th, 1961. A. G. Gray, Wayside Farm, King's Langley, Herts. HERTFORDSHIRE.

November 29th, 1961. A. J. Wright, Red House, Back Street, Garboldisham, Diss, Norfolk. NORFOLK.

November 29th, 1961. T. Buxton, Woodredon Farm, Waltham Abbey, Essex. ESSEX.

November 29th, 1961. R. L. Webb, The Rectory, Garboldisham, Diss, Norfolk. NORFOLK.

November 29th, 1961. G. C. Moule, Park Farm, Market Weston, Diss, Norfolk. WEST SUFFOLK.

November 30th, 1961. G. A. Davey, The Evergreen Oak House, Thelnethan, Diss, Norfolk. WEST SUFFOLK.

November 30th, 1961. Mrs. W. E. Gordon, Isle of Wight Farm, Gerrards Cross, Bucks. BUCKINGHAMSHIRE.

November 30th, 1961. Messrs. W. C. Blacklocks, The Bays, Lydd, Kent. Disease at: Whitehall Farm, Lydd, Kent. KENT.

December 1st, 1961. C. Coomber, Farm View, Hythe End, Wraysbury, Staines, Middlesex. Disease at: Homestead Farm, Hythe End, Wraysbury, Staines, Middlesex. BUCKINGHAMSHIRE.

December 1st, 1961. J. Sunderland, Dartmeet, Toms Lane, King's Langley, Herts. HERTFORDSHIRE.

December 1st, 1961. A. W. Bird, Hither Farm, Thorley, Bishop's Stortford, Herts. HERTFORDSHIRE.

December 1st, 1961. Miss Lambert, The Flacklands, Carleton Rode, Norwich, Norfolk. NOR 03X. NORFOLK.

December 1st, 1961. J. G. Talbot, Hollow Lane Farm, Market Weston, Diss, Norfolk. WEST SUFFOLK.

December 2nd, 1961. C. S. Greatney, The Firs, Ballbar, Hatfield, Herts. HERTFORDSHIRE.

December 2nd, 1961. B. J. Gooderham, Elmwood Poultry Farm, Kenninghall, Norwich, Norfolk. NOR 06X. NORFOLK.

December 2nd, 1961. The Managers, Redhouse Farm School, Buxton, Norwich. NOR 61Y. NORFOLK.

December 2nd, 1961. G. C. C. Shields, South Park Farm, Uphatherley, Cheltenham, Glos. GLOUCESTERSHIRE.

December 2nd, 1961. Mrs. J. W. Rain, Garden House, Market Weston, Diss, Norfolk. WEST SUFFOLK.

December 4th, 1961. R. J. Wood, Curtis Orchard, Upton St. Leonards, Glos. Disease at: Dutch Farm, Shurdington, Cheltenham, Glos. GLOUCESTERSHIRE.
December 4th, 1961. Flowerdale Farms Ltd.; Flowerdale, The Reddings, Cheltenham, Glos. GLOUCESTERSHIRE.
December 4th, 1961. L. W. Nunn & Sons, Grange Farm, North Lopham, Diss, Norfolk. NORFOLK.
December 4th, 1961. R. Johnson, Englemere, East Hampstead, Bracknell, Berks. BERKSHIRE.
December 4th, 1961. H. Gedge, Lilac Farm, Bunwell, Norwich, Norfolk. NOR 01X. NORFOLK.
December 4th, 1961. P. C. Roe, Nowton Hall, Nowton, Bury St. Edmunds, Suffolk. WEST SUFFOLK.
December 4th, 1961. R. Stevens, Primrose Farm, Priors Hill, High Wycombe, Bucks. BUCKINGHAMSHIRE.
December 4th, 1961. J. Lyon, Common Farm, Fersfield, Diss, Norfolk. NORFOLK.
December 4th, 1961. J. W. Brewster, Hill Farm, Banham, Norwich, Norfolk. NOR 05X. NORFOLK.
December 4th, 1961. C. K. Frost, Casa Mia, North Lopham, Diss, Norfolk. Disease at: Dale House, North Lopham, Diss, Norfolk. NORFOLK.
December 4th, 1961. G. P. Hardon, Sunfield Farm, Badgeworth Lane, Shurdington, Cheltenham, Glos. GLOUCESTERSHIRE.
December 4th, 1961. F. H. Cock, Prestbury Park Farm, Cheltenham, Glos. GLOUCESTERSHIRE.

Swine Fever

November 28th, 1961. C. F. Lister, Croome House Farm, Sledmere, Driffield, Yorks. YORK, EAST RIDING.
November 28th, 1961. B. Cadjot, 51, Grafog Street, Port Tennant, Swansea, Glam. Disease at: Piggeries, Kilvey Hill, Port Tennant, Swansea, Glam. COUNTY BOROUGH OF SWANSEA.
November 28th, 1961. A. A. Povey (Manager, Tottenham Piggeries), Town Hall, Tottenham, N.15. Disease at: Piggeries, Markfield Road, Tottenham, N.15. MIDDLESEX.
November 29th, 1961. W. Gill, Belmont, Gt. Lime Road, West Moor, Long Benton, Newcastle upon Tyne, 7. Disease at: Piggeries, Old Factory, West Moor, Long Benton, Newcastle upon Tyne, 7. NORTHUMBERLAND.
November 29th, 1961. A. Seaman & Sons Ltd., Church Farm, Hindolveston, Dereham, Norfolk. NORFOLK.
November 29th, 1961. H. F. Mills & Son, Rosenhurst, Park Lane, Bewdley, Worcs. Disease at: Upper Blackstone Farm, Bewdley, Worcs. WORCESTERHIRE.
November 30th, 1961. H. E. Shaw, Windrush Farm, Minster Lovell, Oxford. OXFORDSHIRE.
December 1st, 1961. H. Metcalfe, Hutton Hill, Ripon, Yorks. Disease at: Derwent Cottage Farm, North Driffield, Selby, Yorks. YORK, EAST RIDING.
December 1st, 1961. J. Hemmings, The Woodyard, Meriden, Coventry, Warwicks. Disease at: Piggeries rear of The Laurels, Birmingham Road, Meriden, Coventry, Warwicks. WARWICKSHIRE.
December 1st, 1961. P. E. Tuckey, The Green, Meriden, Coventry, Warwicks. WARWICKSHIRE.
December 4th, 1961. C. Patrick, Eau Withington Court, Withington, Hereford. HEREFORDSHIRE.
December 4th, 1961. C. J. Stephens, Lorne House, Kingsland, Leominster, Hereford. HEREFORDSHIRE.
December 4th, 1961. K. Bartl, 48, Newton Lane, Wigston, Leicester. LEICESTERSHIRE.
December 4th, 1961. E. Cameron, Lochearnhead Hotel, Lochearnhead, Perthshire. PERTHSHIRE.
December 4th, 1961. B. Buckingham, Petersons House, Petersons Lane, Aylsham, Norwich, Norfolk. NOR 07Y. Disease at: Bure Poultry Farm, Sir Williams Lane, Aylsham, Norwich, Norfolk. NORFOLK.

As from our issue of January 6th, 1962, we shall revert to the former practice of publishing these lists in county order.

Letters to the Editor

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

GENERAL

Neonatal Scouring in Piglets

Sir,—We were pleased to read in your columns of the issue of November 25th, 1961, the letter by Smith and Jones that they had up to present found no strains of *Escherichia coli* resistant to neomycin therapy.

Neonatal scour in piglets is a serious problem in this practice, especially in one herd of 90 breeding sows where management and buildings are first class. A severe outbreak of neonatal scour occurred in June of this year and the usual forms of therapy, *viz.* sulphonamide, streptomycin, tetracyclines, chloramphenicol, and nitrofurans, proved virtually of no avail.

Two hundred mg. neomycin in a paste by mouth gave spectacular results both therapeutically and prophylactically and up to date has still done so. However, after consultation with the manufacturers of the neomycin paste, we realised our dosage was too high, with the result that at present all piglets receive 100 mg. at birth. Individual piglets are treated later in a similar manner if they show any symptoms of scouring.

Having obtained successful prophylaxis, we left one litter of 7 piglets untreated as a control, and within 72 hours all piglets had died, and *E. coli* was recovered from heart blood and bone marrow.

Taking into account the previous heavy mortality, the total loss of the control litter, and the success of the drug as a prophylactic agent, the pig breeder is not as yet prepared to cease administration of neomycin at birth.

In view of our previous experience with antibiotics and *E. coli*, the report by Smith and Jones is most encouraging; but as sceptics, we consider resistant strains will ultimately develop, though the exclusion of the drug from animal feeding-stuffs will prolong its efficacy.

Acknowledgment.—We should like to thank the Veterinary Research Department, Boots Pure Drug Co. Ltd., Thurgarton, Notts., for supplying the neomycin paste and also for their help and interest.

Yours faithfully,

ALASDAIR STEELE-BODGER.
MATTHEW SEMPLE.
H. E. DAVIES.

10, Bore Street,
Lichfield,
Staffs.

December 1st, 1961.

Sir,—I should like to confirm the statement made by Williams Smith and J. E. T. Jones in THE VETERINARY RECORD of November 25th regarding the

sensitivity of *Escherichia coli* to neomycin. In experimental work here on faecal coli this antibiotic has been administered orally to a large number of litters of normal piglets. A close check has been kept on the sensitivity of the faecal coli flora but no coliforms resistant to neomycin have ever been isolated, although the antibiotic has been in intermittent use over a period of a few years on the same premises. This is contrary to our experience with streptomycin and Aureomycin where resistant coliforms have appeared sometimes within a week of the antibiotic being used for the first time, and in the case of Aureomycin the resistant types seem able to persist on the premises.

Single daily doses of 100 mg. neomycin sulphate, given orally, have reduced faecal coli in healthy week-old piglets from hundreds of millions to < 1,000 per gramme. There have been no outbreaks of neonatal scours on our own premises so that we have been unable to carry out controlled clinical trials using neomycin but we have received reports of its successful use by veterinary surgeons in the field for treating scours in baby piglets, sometimes when the condition had failed to respond to other antibiotics. These outbreaks have been assumed by the practitioners to be due to *E. coli* infection, though unfortunately there has been no opportunity of confirming this bacteriologically.

The failure of neomycin to induce resistance in coliforms should make it a particularly suitable antibiotic for trial under intensive housing conditions.

Yours faithfully,
L. H. AYNSLEY.

Boots Pure Drug Co. Research Dept.,
Veterinary Science Division,
The Priory,
Thurgarton,
Notts.
November 28th, 1961.

Veterinarians' Fees

Sir,—May I as a member of the public intrude on your columns to make a plea which I feel will help avoid a repetition of the sort of misunderstanding which recently occurred between myself and my veterinary surgeon?

I recently took a dog to the surgery to be booster vaccinated and received an account which was very considerably in excess of the initial vaccination for which another veterinarian visited my premises twice. The account read, "to professional services for the month of . . ." and the sum charged. No more. I naturally fairly forcibly queried the discrepancy in charges, and received a detailed (but somewhat aggrieved) reply outlining the standard charges agreed with the B.V.A.* I am now quite satisfied, the bill is paid, and relations (on my side anyway) have, I hope, returned to normal; but the profession nearly notched up another client with an "overcharging grudge." Had some mention been made of the standard agreed charge this whole matter would never have arisen.

Please, Sir, persuade your members to provide an *itemised* or detailed account, as does everyone else who has occasion to send me the perishing things!

Yours faithfully,
J. N. GADD.

362, Loughborough Road,
West Bridgford,
Nottingham.
November 16th, 1961.

* Presumably our correspondent's statement about standard charges referred to the recommendation made by the Midland division of the B.S.A.V.A. The B.V.A. has made no agreement as to standard charges.—*Editor.*

The British Veterinarian and the Common Market

Sir,—Those of us still working in Africa have been long aware of the debt owed by African stock-owners to our colleagues trained in Europe. Continental veterinarians have enabled emerging and emergent African states to fill posts previously held by British veterinarians, and salaries and conditions of service apparently unattractive to members of the Royal College of Veterinary Surgeons are accepted by continental veterinarians.

On Wednesday, November 15th, *The Times* published a forecast by Sir Wilfred Fish, President of the General Dental Council, that a professional man legally entitled to practise in one member-state of the European Common Market will be able to practise in any of the others. Apparently the Treaty of Rome provided for the progressive abolition, over 10 years, of restrictions on the free practice of professions throughout the European Economic Community. Experience in Africa suggests that a surplus of continental veterinarians exists. How stands the British veterinary profession?

Yours faithfully,
G. R. SCOTT.

Whiteholm,
Gullane.
November 16th, 1961.

[We understand that the Royal College of Veterinary Surgeons, earlier this year, drew the attention of the appropriate Government authorities to the portion of the Treaty of Rome which deals with the professions. However, like many portions of the Treaty, what might appear to be a basic right can be hedged about by conditions which would reduce the effectiveness of the general principle. It would appear that any action regarding the medical, pharmaceutical and veterinary profession requires a unanimous vote of all the member States. There is also provision in the Treaty that activities which include "the exercise of public authority" remain the responsibility of each country.—*Editor.*]

The V.V.B.F. and Covenants

Sir,—The Editorial in your issue of November 25th expresses very clearly the value of this Fund to all members of our profession. Only those can fully appreciate it who have experienced the sudden and unexpected economic catastrophe that can overtake a family as the result of illness or death of the breadwinner, or some other equally unexpected mis-

fortune. You have drawn attention to the greatly increased value to the Fund, of a covenanted subscription with no extra cost whatever to the subscriber. May I further point out to anyone who hesitates to involve himself in a promise to continue for 7 years, that should some misfortune prevent him completing this contract, the only possible reaction would be that the Fund might have to surrender the amount of tax which had been recovered under this particular agreement. Experience shows, however, that the Inland Revenue is not usually unsympathetic in such rare cases. What is quite clear, without any doubt, is that the Covenanter is not involved in any sort of repayment, or obligation to continue his subscription in such an unlikely and unfortunate circumstance.

Yours faithfully,
E. P. BARRETT.

28, Stoke Road,
Guildford,
Surrey.
November 27th, 1961.

SCIENTIFIC

Polioencephalomalacia in Calves

Sir,—The recent report by Howell (1961) of cases of polioencephalomalacia in calves in Britain is of considerable interest to us, as we have observed 9 possible cases of the disease on 5 Northern Ireland farms since August of this year. The condition is relatively uncommon and was certainly new to us when the first cases were brought to our notice. Its symptoms and pathology have been studied and are briefly recorded here, together with the results of transmission tests. The aetiology of the disease is still unknown and it is felt that the more information accumulated from field and laboratory studies the sooner will the possible cause be found. The conditions observed by Howell, by Terlecki and Markson (1961), and by us are remarkably similar and are probably related.

Nine suspect cases were brought to our notice between August 1st and October 12th, 4 being on one farm, 2 each on 2 other farms, the remaining one being a single case. Eight died and necropsies were carried out on 5 of these. One animal showed a complete clinical recovery.

Clinical symptoms. The onset of symptoms in each case was rapid, commencing with dullness and inappetence, apparent blindness, nervousness and muscular inco-ordination. Within 12 to 36 hours the animal was usually recumbent and opisthotonus an outstanding symptom. The calf was capable of kicking with great force in a convulsive manner even when recumbent. Death occurred within 2 to 6 days. Less constant symptoms were grinding of the teeth and uncontrolled eye movements; in 2 calves a mild scouring was observed and in one constipation. Temperatures were always normal.

Diagnostic tests. Faeces and kidney estimations for lead were normal; serum calcium and magnesium levels were within normal ranges; white and red blood cell counts showed no unusual features and an *E. coli* and streptococcal infection was cultured from one brain only, the other being sterile.

Pathology. Meningeal congestion and excess cerebro-spinal fluid were present in every specimen at autopsy, but cortical discoloration as described by Howell and by Terlecki and Markson was less prominent and was recognised confidently in only 2 cases. Petechiae were evident in the cerebral cortex in 2 calves. The outstanding histological feature was the presence of focal or laminar areas of spongy transformation (microcavitation) in the cerebral cortex, particularly in the region of the occipital poles. The neurones within these zones were shrunken, hyperchromatic, degenerate structures lying within rounded vacuoles. Neuronal degeneration was also evident in areas where microcavitation was absent. There was a striking absence of cellular infiltration in the affected areas of the cortex but macrophage exudation into the overlying meninges was frequently marked. Capillary vasculitis was present in many sections of the cortex and in the subcortical white matter in some areas. Primary lesions were not observed in the corpus medullare but in some severely damaged convolutions there was perivascular infiltration in the central white matter. The brainstem and spinal cord were not involved but in 3 cases changes were present in the cerebellar cortex. These lesions appeared to be confined to the vermis and consisted of foci of necrosis involving the granular layer and in some instances, the adjacent Purkinje cells.

Transmission. V.S.B.S. mice inoculated intracerebrally with 10 per cent. brain suspended in 0.75 per cent. bovine albumen in phosphate buffered saline of pH8 remained normal until they were destroyed on the 28th day. No cytopathic effect occurred in embryo calf or Rhesus monkey kidney monolayers inoculated with whole blood, faeces and nasal and oral secretions from both affected and in-contact animals. Calves inoculated subcutaneously, intravenously, intraperitoneally and epidurally remained normal for 21 days and lesions were not detected when they were destroyed.

It is of interest to note that 5 years previously on one of the affected farms, lambs of 4 to 10 days old showed symptoms similar to those observed in the calves. Since starting this letter, we have encountered encephalomalacia in a group of 16-week-old pigs dying after a short illness. Here, again, no aetiological factor has been discovered.

Yours faithfully,
C. DOW,
J. K. L. PEARSON,
J. E. F. RANKIN.

Veterinary Research Division,
The Farm,
Stormont,
Belfast, 4.

J. B. McFERRAN.

Department of Microbiology,
The Queen's University of Belfast.
November 28th, 1961.

References

HOWELL, J. McC. (1961). *Vet. Rec.* **73**. 1,165.
TERLECKI, S., & MARKSON, L. M. (1961). *Ibid.* **73**. 23.